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August 3 1973

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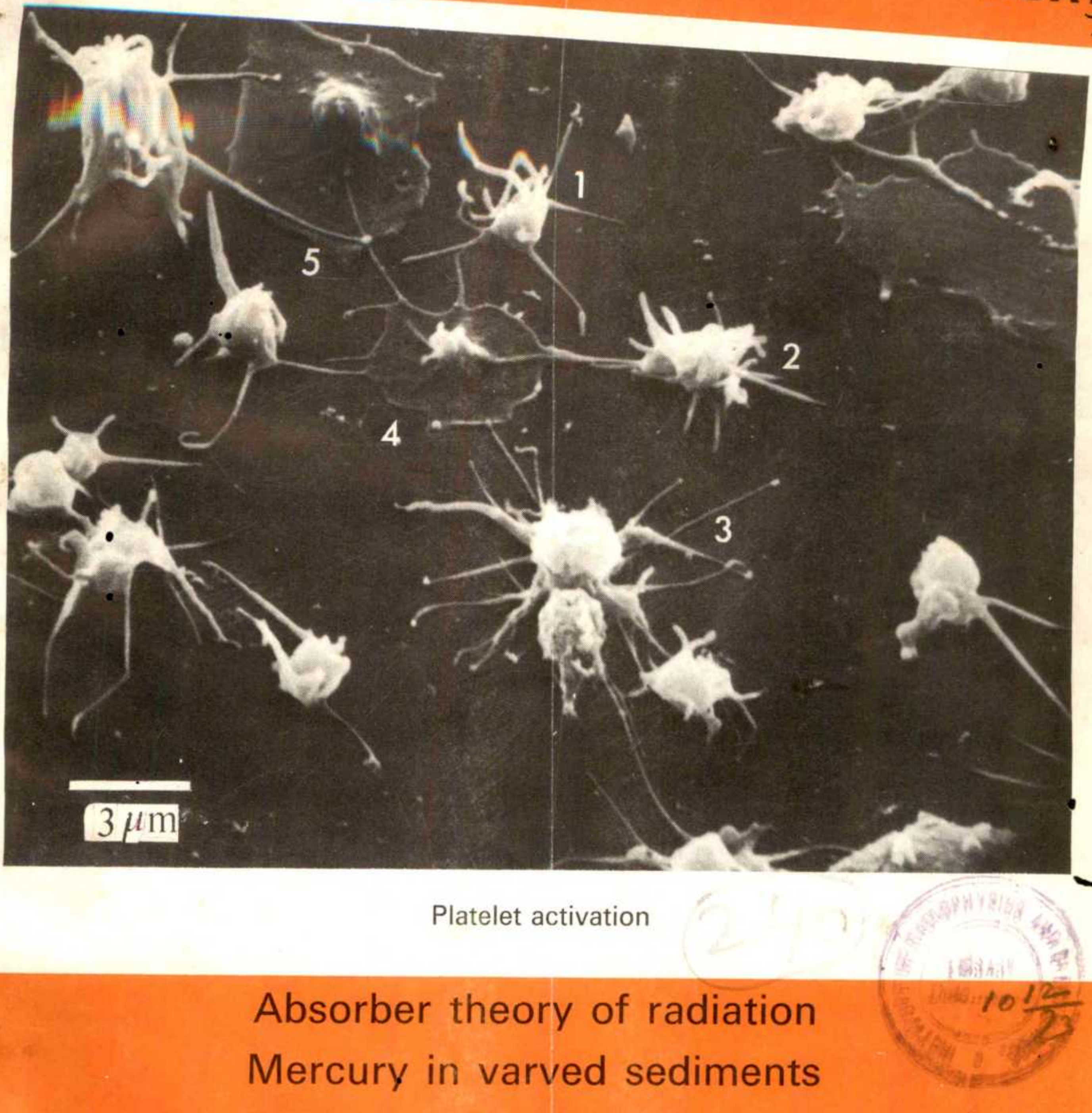

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D. F. Horne, M.B.E.

Lecturer, Cranfield Institute of Technology
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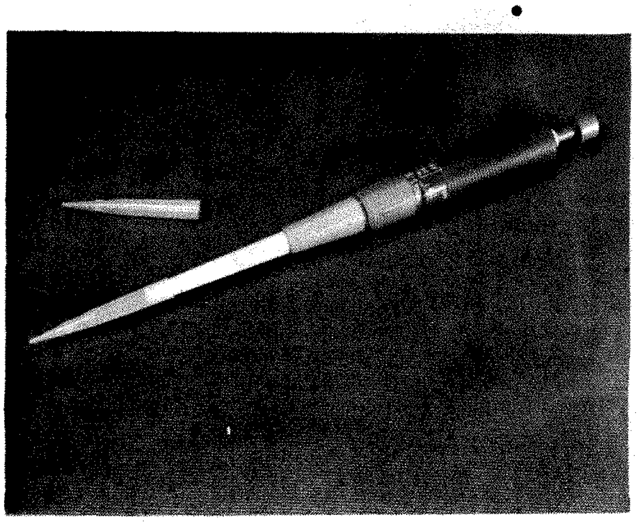

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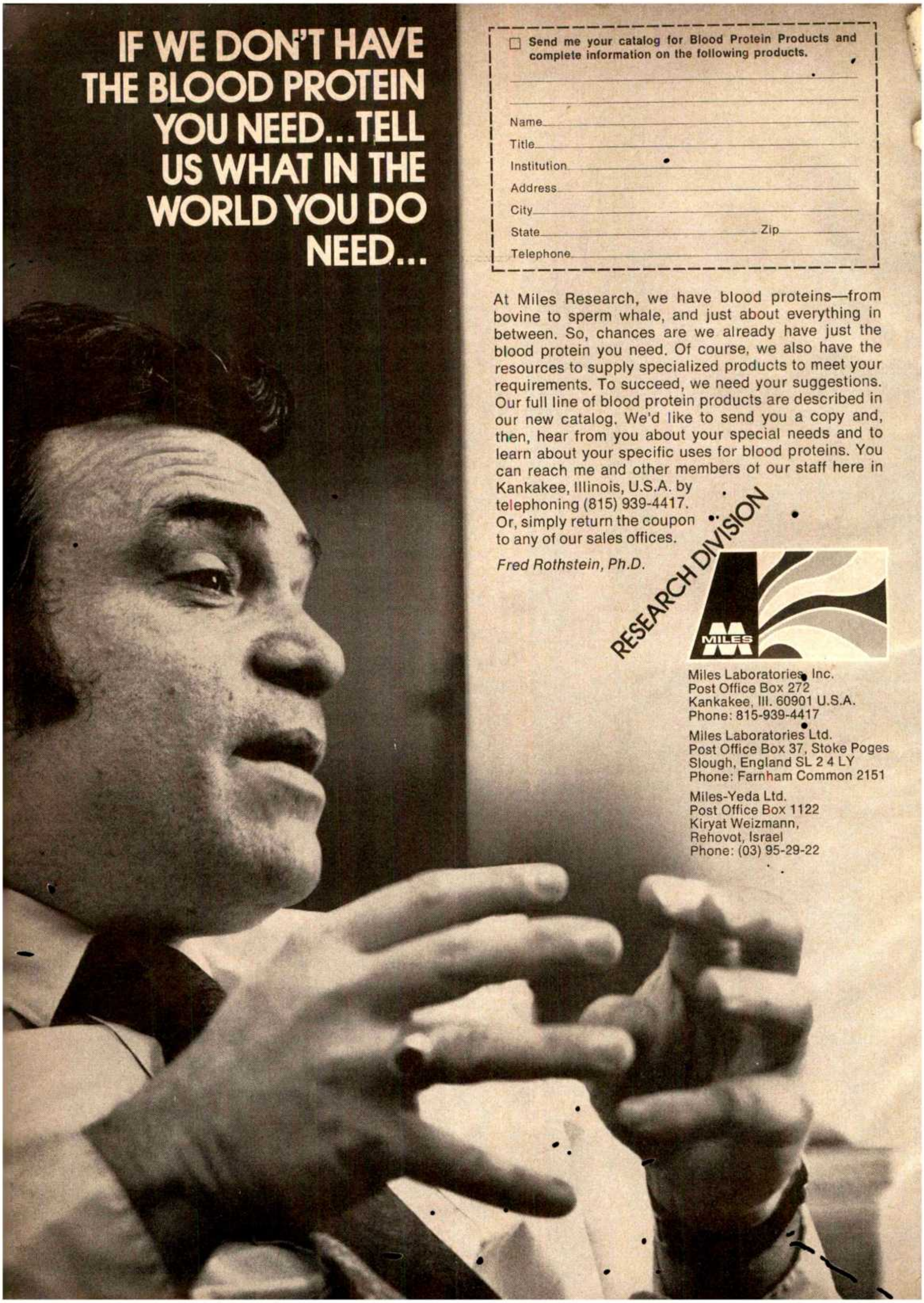

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AUGUST 3 1973

Costs and Benefits of Clean Air

THE Organisation for Economic Cooperation and Development specializes in producing reports, but the organization's latest document, which sets out to assess the effects of an increased demand for energy on the environment, is out of the ordinary in that it is both lucid and a mine of useful information on sources of energy (*Report and Conclusions of the Joint* ad hoc *Group on Air Pollution from Fuel Combustion in Stationary Sources*, OECD, Paris, 1973). This, however, makes the report no different from several others which have appeared recently in what might be called energy concern year But the intriguing aspect of the OECD document is a calculation of the likely costs needed to keep the level of gaseous pollutants from these sources at the same level in 1980 as it was in 1968, the base year for the OECD calculations Between 1968 and 1980, according to all estimates, there will be a two thirds increase in total fuel consumption in most of Europe and in North America, while Japan during this period will increase its consumption by almost 230% And if no action is taken to abate the gaseous pollutants from power stations and other industrial sources the level of these pollutants will increase by 70% by the end of the decade

During the next ten years the price of all fuels, except possibly uranium and plutonium for nuclear power generation, will inexorably rise And equally inexorably there are going to be pressures applied, quite properly, to keep the exhaust fumes from power stations and industry as clean and free of sulphur dioxide and nitrogen oxides as possible But what increase in fuel costs should be tolerated in order to maintain the environment in its present state? There is no point in pretending that the consumer will not pay the increase in the end, for in spite of the often enunciated principle that the polluter must pay, the cost will appear on the electricity or gas bill, on the price of the product, or in some cases as an increase in taxes But the news from the OECD is cheerful enough this time Only an estimated 2.5% to 5% increase in fuel costs is necessary to keep sulphur dioxide emissions constant for the next few years Such an increase is, of course, much less than the expected increase in fuel prices in the same period, and for once, the benefits of this increase in cost would seem to clearly outweigh the disadvantages

But sulphur dioxide emissions do not constitute the entire story Nitrous oxides and dust are also emitted from industrial stacks and the report does not consider the pollutants emitted from internal combustion engines Unfortunately, the way in which nitrous oxides, which are one of the chief pollutants in car exhausts, contribute to chemical reactions in the atmosphere is not completely understood And because of this the best way to treat these gases before they are emitted to the atmosphere is a contentious topic But the technology is now available, at a cost, to reduce the amount of these oxides emitted even if little is known about how the oxides cause problems Although the cost of keeping sulphur dioxide emissions at a low level is modest when expressed in terms of the total spent on fuels it still means a capital investment of anything up to $15,600 million, a not insubstantial sum, in the next few years and the annual extra operating costs would run to between $2,200 million and $4,200 million But the OECD report raises the question of whether individual countries should decide to try and return the pollutant levels to those existing in 1968, or whether this should be an international approach The OECD points out that it is feasible to control the amounts of sulphur dioxide emitted but the wider aspect is whether it is sensible to attack one part of the problem of air pollution while ignoring other substances which are being continually emitted into the environment. Certainly sulphur dioxide emissions should be contained within reasonable limits, but it is surely not fair that industries which burn fuels with a high sulphur content should be made to wear environmental halos while other industries which pollute in a different way should have no strictures put upon them What is surely needed is an overall policy, similar to that for which the European Economic Commission has pleaded, which does not favour one side of industry over another

---

100 Years Ago

Telescope Tube for Celestial Photography

I HAVE not yet seen any satisfactory plan suggested of getting over the difficulty experienced in celestial photography by the expansion and contraction of telescope tubes, by changes of temperature in metal tubes

I therefore venture to suggest the following plan, which may be so arranged as to keep the object-glass and camera-slide *exactly* the same distance apart, and so keep the true focus when once found The arrangement would have to be modified according to the metal of which the tube is made, but taking a brass one (the most common), with the camera attached to the eyepiece-slide, the correction will be effected by attaching to the main tube, near the eyepiece, two zinc rods the length of the main tube, upon which they must rest loosely, to the free ends of these, near the object-glass, attach a rod of iron extending to the eye tube, let this iron rod be attached to the eye-tube when the sensitive-plate is exactly in focus, any change in temperature will then have no effect on the focus, for the expansion and contraction of the three metals will keep the distance from object-glass to sensitive-plate constant All who have worked with a telescope giving sharp definition, will know that this is not an unnecessary precaution, as it may seem to some.

Sydney Observatory, June 14 H. C. RUSSELL

From *Nature* 8, 284, *August* 7, 1873

OLD WORLD

The Research System as Margaret Thatcher sees it

FURTHER support for the formation of a European Science Foundation came from Mrs Margaret Thatcher, Secretary of State for Education and Science, in a recent address to the Parliamentary and Scientific Committee

Mrs Thatcher said that increasing collaboration between European scientists creates the need for a "forum in which projects and ideas can be explored and exchanged" It is therefore "highly significant and encouraging that discussions which have been going on for the past few months between the research councils and academies of western Europe with the active participation of the European Commission seem likely to lead to the formation of an independent European Science Foundation to provide just such a forum"

Mrs Thatcher's public approval of the proposed foundation follows on that of Sir Brian Flowers, chairman of the Science Research Council, who recently declared that the formation of the foundation is now "inevitable" (see *Nature*, **243**, 254, 1973) Like Sir Brian, Mrs Thatcher went on to emphasize that the "big sciences' would not always be the principal beneficiaries of such a foundation "I am not keen on cooperation merely for its own sake But I do feel that if scientists are given support and opportunities to meet together in their own fields, there will be no shortage of worthwhile suggestions of good scientific merit, even though maybe of modest cost, for joint activity," she said

Mrs Thatcher also discussed the changes that have followed from last year's white paper on *A Framework for Government Research and Development* The white paper recognized, Mrs Thatcher said, that "scientific activity is one and indivisible Much basic research will involve a capability for applied research and *vice versa* It would therefore be a simple-minded view to say that the intention of the white paper was to assign responsibility to customer departments for the support of applied scientific research, and to regard fundamental science as an area in which the concerns of the government played no part The reality is much more complicated Some broad divisions can be made for the purpose of funding, but to my mind a more important feature of the white paper is the closer association of executive departments with the totality of the research council's work"

"The essence of the research council system," Mrs Thatcher went on, "is that scientific judgments should be made by scientists and defended against the challenge of fellow-scientists This is unchanged by the fact that scientists drawn from government now play a part"

Discussing the role polytechnics are to play in research, Mrs Thatcher said their research "will be different both in nature and degree" Polytechnics may undertake some fundamental research, Mrs Thatcher said, as they may have particular expertise in certain subjects, but they "are and will remain" primarily teaching institutions "While it would be right that their staff should engage in

---

BRITISH ASSOCIATION

Brighter Outlook

THE British Association for the Advancement of Science is shortly to launch an appeal for £15,000 Several hundred companies and charitable trusts are to be approached in the hope that they will agree to sponsor a wide range of the association's activities

The proposed appeal is announced in the association's annual report published last week, and this week Mr Alec Hughes, an assistant secretary with the association, said that the intention is to invite companies to attach their names to particular activities and events in the association's calendar Items for which the association is seeking support are the British Association Student Scientists conference planned for London in January next year, a full range of the British Association for Young Scientists activities, and the study groups that the association is setting up to examine "topics of urgent public and scientific moment"

The other prong of the BA's campaign is to approach universities, through their vice-chancellors, to ask their support What the BA is looking for is both facilities for the association's branches to hold meetings, and some sort of active help from the universities in encouraging academics to join the association One form this might take is the appointment of an official association representative on each campus As Mr Hughes says, "the association's objectives in the advancement of science should be significant to the universities"

Although the target of the appeal is £15,000, only about a third of this is expected to be raised in the coming year It is hoped that by inviting companies to sponsor particular events the response may be better than that which might meet a general appeal for money for unspecified purposes

In spite of the decision to launch an appeal the association's finances continue their recovery after the deficits of recent years This year the accounts show a surplus of £2,242 on an expenditure of £48,792 The improvement is still largely due to administrative economies Headquarters staff has been reduced to fewer than ten full-time administrators as against 24 two years ago The move to more compact premises in Savile Row has also helped

Sir Eric Mensforth, the association's treasurer, predicts that income will rise to £54,000 in 1973–74 "which should permit some welcome expansion in activities"

Membership expanded by 200 during the year to 1,900 members plus some 6,000 BAYS members, while plans to involve more students in the BA went ahead This year's annual meeting is due to be held in Canterbury from August 20 to 24 The programme—on the face of things rather more stimulating than last year's—includes symposia on the exploration of the sea, on reserves, utilization and re-cycling of mineral wealth and one on Kent and Europe Whales, oil pollution of the sea, earth resources satellites, the social responsibility of scientists and the future of weather forecasting will all be discussed, while Professor Kenneth Mellanby promises to demonstrate how almost all changes made by the government to improve the efficiency of research between 1945 and 1973 have been counter productive Sir Kingsley Dunham's presidential address is on the advancement of environmental science

As an experiment to encourage other learned societies and their members to become involved in the association's work the Challenger Society, the Geological Society of London, the Geologists' Association and the Estuarine and Brackish-Water Science Association are officially participating in some of the sessions research to strengthen their teaching abilities, I envisage the main research effort as being in a field to concern industry, business and the public services, often in a regional or even a local context. The universities will thus continue to be the main repositories of pure research conducted with the cultural aim of the advancement of knowledge for itself."

RESEARCH COUNCILS

New Chairman for NERC

Sir Peter Kent is to succeed Professor F. H. Stewart as chairman of the Natural Environment Research Council from October 1. Sir Peter, 60, who was knighted this year, is a former exploration manager and chief geologist of British Petroleum. His appointment is for a period of four years.

Sir Peter is no stranger to science policy. From 1968 until it was disbanded he was a member of the Council for Scientific Policy and he is currently an independent member of the Advisory Board for the Research Councils.

Sir Peter Kent

He comes to the Natural Environment Research Council at a time when it is having to adjust to the large scale reorganization of its work that emerged from last July's white paper on government research and development. Sir Peter was a member of the working group that produced the Dainton report on the research councils—which recommended a rather more evolutionary change in the relationship between the research councils and government departments than the large scale transfers of funds that Rothschild proposed and the government, after amendment, accepted. This year £2.25 million of the council's £15.3 million budget (1971–72 prices) were transferred to the Department of the Environment and the Department of Trade and Industry. A further £3.25 million and £4.5 million will have to be found in 1974–75 and 1975–76.

Sir Peter's experience with BP—which he joined in 1936—makes him well aware of the basic problems in geology and oceanography, as well as giving him an insight into the workings of industry that few academics achieve.

Sir Peter is a graduate of the Universities of Nottingham and London, a fellow of the Royal Society and a member of its council since 1968. While with BP he was responsible for geological survey work in Iran, East Africa, Papua, Canada, Alaska and Britain including the North Sea.

RADIOACTIVE WASTE

Safe in the Sea

Reassurance that the dumping of radioactive waste at sea is safe is given in a report issued yesterday by the National Radiological Protection Board.

Dr G. A. M. Webb and Dr F. Morley have built a model to evaluate how radioactive waste disposed of in the deep ocean is dispersed with time. By making all kinds of unlikely assumptions about the worst possible conditions for disposal, they confidently conclude that up to several thousand and, for some types of activity, several million times the quantity of radioactivity now disposed of in this way could be deposited on the sea bed without the dose limits recommended by the International Commission on Radiological protection being violated. Not only are the amounts of activity now being disposed of by Britain and other countries in this way negligible by comparison with the maximum allowed amounts, but Dr Webb and Dr Morley also point out that radioactive waste could be disposed of in the sea for several thousand years without there being any adverse effects.

A basic assumption made in the model is that the waste is dropped into deep water in packaged drums and that the drums reach the sea bed without any of the activity leaking out. In practice these drums are not airtight to ensure that during descent the pressure inside the drum remains the same as that outside so that there is no danger of the drum fracturing before it reaches the sea bottom. The different types of radioactivity are considered separately. The Harwell scientists assume that the tritium in the waste is released immediately the drum reaches the ocean floor whereas in practice it will probably take the tritium several years to percolate out of the drum. It is also assumed that all other waste will gradually leak out within ten years although it is suspected that drums will retain their soluble waste for up to tens or even hundreds of years and indeed much of the waste could languish in the drums for much longer than that.

But the most significant assumption made is that the activity once released will not deposit onto sediments on the sea floor and that it will diffuse throughout the ocean. In practice most of the activity would be removed in this way and little would be left to be circulated.

Britain at present disposes of at most 20,000 curies of radioactive waste in the sea bed every year, of which only about 100 curies are due to alpha activity. According to the model it would be perfectly safe to deposit up to 10^{10} curies of alpha particle waste based on ^{239}Pu every year and up to 10^6 curies based on ^{226}Ra. Up to 10^{11} curies of general beta and gamma active waste could also be dumped with 10^{15} curies of tritium as well.

SPACE

Mars Soft-lander?

from our Soviet Correspondent

The launch of Mars-4 and Mars-5, the latest Soviet Mars probes, on July 21 and 25, was announced with the usual reticence about their programmes. The official TASS press releases stated simply that their main aim was to continue "the scientific investigations of the planet Mars and its ambient space begun by the Mars-2 and Mars-3 probes in 1971", two probes "analogous in structure and purpose" are being used so that "simultaneous scientific investigations" . . . may "permit more complete data to be obtained". This does not imply, however, that the two probes are entirely identical.

The Mars-2 and Mars-3 probes, coming as they did almost ten years after the Mars-1 flyby, carried out an interesting series of synchronized observations of surface and atmospheric features from different orbits (that of Mars-2 being near-circular and Mars-3 highly elliptical).

It is difficult at this stage to estimate how the new probes will "continue" the programme. So far, the Soviet space planners have avoided straight-forward repetition of a successful project—thus Lunokhod-2 differed from Lunokhod-1 in carrying magnetic experiments and in traversing a far wider survey area. It seems likely, however, that some soft-landing attempt may be made. Whether this would be a simple physico-chemical instrument package, or one of the more exotic automated exobiology experiments or the roving "Marsokhod" that has been mentioned in the Soviet press, will probably remain a mystery until the probes reach Mars in February, 1974.

NEW WORLD

Fusion Power Changes Gear

by our Washington Correspondent

THE past year has been a very good one for fusion research in the United States. So good, in fact, that officials in charge of the programme at the Atomic Energy Commission are predicting that a demonstration commercial fusion power reactor will be operating by the mid-1990s—a five year improvement on their previous predictions. The factors which have led to such a rosy outlook are a run of successes in the research programme which have led to a recent reorientation in planning, and most important, the possibility of a huge increase in the AEC's budget for such research in the next few years.

That, in any case, was the line taken last week by a string of witnesses before the Joint Committee on Atomic Energy, which held its second set of hearings in two years on the AEC's fusion research programme. In the previous hearings, AEC witnesses were optimistic about the future for fusion power (see *Nature*, **234**, 120; 1971); this time they were positively enthusiastic, and their enthusiasm has been translated into plans to burn a fusion fuel of deuterium and tritium much earlier than they were estimating just a year ago.

Dr Roy L. Hirsch, Director of the AEC's Division of Controlled Thermonuclear Research, told the Joint Committee last week of a meeting of leaders of the programme held in mid-July, at which the outlines of the accelerated programme were agreed to. The chief change from previous plans is to push ahead with the design of equipment and experiments to burn a fusion fuel without first waiting for a demonstration that the physical conditions necessary to achieve a fusion reaction are scientifically feasible.

The ultimate goal of fusion research is to produce energy by imitating the processes that take place on the surface of the Sun. The idea is to heat a mixture of heavy isotopes of hydrogen—initially deuterium and tritium—to about 100 million degrees, and to contain the hot plasma out of contact with solid surfaces long enough for hydrogen ions to fuse together to form helium nuclei. The reaction would release energy and neutrons.

The previous plans called for a four-stage research and development programme to reach that goal. Phase one—the present phase—is physical research on methods of heating plasmas and confining them. The next stage is to build experiments to demonstrate that it is scientifically feasible to reach the physical conditions of temperature, density and confinement time necessary to get net energy out of fusion reactions. This stage would involve research on hydrogen, which would not actually undergo fusion. The third step is to build a test reactor in which deuterium and tritium would be allowed to react to produce net energy output. And the final stage is the construction of a prototype commercial reactor. The new plan is to combine the second and third stages, a move which Hirsch said last week "reflects our growing belief that our successes indicate that scientific feasibility is not the milestone technical issue it was once thought to be".

Among the successes to which Hirsch referred are considerable advances in the past two years in the field of magnetically confining plasmas, but perhaps the most exciting breakthrough came early in July at Princeton's Adiabatic Toroidal Compressor (ATC), a tokamak machine. Last year, a series of successful experiments on the ATC machine produced good results in heating a plasma by compression, and in addition the density was increased to the minimum thought to be necessary to operate a fusion reactor. More recently, however, the Princeton machine has been used to demonstrate a second heating method known as neutral beam heating.

First developed with the linear mirror machines at the Livermore Laboratory, neutral beam heating consists of injecting a high-energy beam of deuterium ions into the hot plasma. In the Princeton experiment, a plasma was heated to about 2 million degrees in the tokamak by resistance heating, compressed to raise the temperature to about 6 million degrees and then a beam of deuterium ions was fired into it. The trick is first to fire the deuterium ions through a gas so that they pick up electrons to neutralize the charge, which enables the beam to pass unhindered through the magnetic field that contains the plasma. The ATC experiments increased the ion temperature by between 20 and 25 per cent, even though the injected beam was at relatively low energy. "This early result", Dr Melvin Gottlieb, Director of the Princeton Plasma Physics Laboratory, said last week, "is indeed encouraging".

It is perhaps no coincidence that the reorientation of the fusion research programme was agreed to at a meeting which took place less than three weeks after President Nixon's statement on energy. In that statement, Mr Nixon announced that an extra $100 million

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NSF

David's Doubts

by our Washington Correspondent

DR EDWARD E. DAVID JUN., who resigned in January as Science Adviser to the President, expressed some reservations last week about the federal government's new science policy machinery which, he said, has "downgraded in my view, the direct influence of scientists on societal affairs". The new arrangements, announced two weeks after David left the government to become Executive Vice-President of Gould Inc., involve the abolition of the Office of Science and Technology and the transfer of its functions to the director of the National Science Foundation.

Testifying before the House Committee on Science and Astronautics, David suggested that the transfer of science policy responsibilities from the White House to the National Science Foundation has resulted in an "unstable" arrangement because "NSF's history is deeply rooted in the academic style which rightly demands single-minded concentration on scientific excellence to the exclusion of other factors. This characteristic is difficult to leaven with other, less science-based realities".

He suggested that there are two possible resolutions of the instability, the first of which is for NSF to "follow its cultural past and thereby revert to the narrower concerns of science and academic research.... In this role, NSF would be no more than it is now". Alternatively, the foundation "may succeed in transcending its past, and actually achieve the national stature necessary" to carry out its coordinating and advisory functions. That, of course, would mean that the foundation would rise in the Executive hierarchy, since it would have to influence other government agencies concerning programmes which cut across their operating boundaries. "It would also mean", David suggested, "that NSF would serve as the technological beacon for other agencies. It must act as a surrogate for the President to exert these influences". David offered no predictions about which course the NSF will follow.

will be devoted to energy research and development next year and that $10,000 million will be spent on such research over the next five years AEC Commissioner Dr Clarence Larson told the Joint Committee that the fusion programme would fit into the expanded energy research and development programmes, and Hirsch added that he expects the fusion effort to grow over the next few years into a programme costing "hundreds of millions of dollars" Last year, the fusion programme was given some $66 million, this year, it is set to receive some $90 million

As for the balance of the programme, Hirsch said last week that tokamak research will continue to receive about 60 per cent of the funds, while the rest will be evenly divided between research involving mirror machines and the so-called theta pinch machines

In view of the large expenditures envisaged for fusion research, and the optimistic forecasts for commercial fusion power, members of the Joint Committee predictably asked whether priorities in the AEC's budget need to be reassessed In particular, should the commission continue to give the breeder reactor top priority? They received the predictable reply, for Dr Larson pointed out that it is reasonably certain that breeder technology will work, and that there will be full-scale production of power from such reactors by the year 2000 Fusion technology, on the other hand, although promising, is by no means certain, and that even if the goal of a demonstration reactor by 1995 is met, it will probably be another 15 years after that before widespread commercial power production

In that regard, it is perhaps symbolic that while the Joint Committee was conducting its hearings into the fusion programme, Dr Dixie Lee Ray, the Chairman of the Atomic Energy Commission, was in Chicago for the signing of agreements between the government and private industry setting out the responsibilities of each party in the programme to build a liquid metal fast breeder demonstration reactor

In his first energy message to Congress in 1971, President Nixon called the breeder the "best hope" for meeting energy demand, and the goal is to build the demonstration plant, at a cost of some $700 million, by 1978 Following that, the AEC reckons that the reactor will be commercially available by the late 1980s

It has often been argued, however, that by sinking so much money into the breeder reactor, other attractive methods of providing energy have been foreclosed, and in particular, the argument has been raised that fusion research has been held back through lack of money A federal appeals court recently decided, however, that the AEC must file an environmental impact statement on the entire fast breeder programme (see *Nature*, **243**, 431, 1973), which will require the commission to consider alternative methods of producing energy

SCIENCE EXPENDITURE

Budget Battle Continued

by our Washington Correspondent

FOR the best part of a year, Congress and the Nixon Administration have been locked in a constitutional wrangle over which branch of the federal government has the final control over public expenditure Although the issue has been rather overshadowed recently by a more pressing constitutional crisis, the importance of the budget dispute to the scientific community was made evident last week by a set of figures released by the House Commerce Committee In the 1973 fiscal year—which ended on June 30—the Administration failed to spend nearly $1,100 million that Congress had earmarked for health programmes, and the unspent money included some $226 million for research programmes of the National Institutes of Health (NIH)

In fact, as far as NIH is concerned, the Administration totally ignored Congressional mandates and followed its own course of action The situation is complicated by the fact that last year Congress did not pass an appropriations bill acceptable to President Nixon for the Department of Health, Education and Welfare, but, in short, this is what happened After two HEW appropriations bills had been vetoed by Mr Nixon because he considered them inflationary, Congress finally decided that the department should be funded according to a continuing resolution Such a resolution directs the Administration to fund any given HEW programme at the smallest level contained in one of three measures HEW's budget for the previous year, the Administration's original budget request for 1973, or the vetoed bill In the event, however, the Administration simply used a different measure—a revised budget request which, for the health programmes of HEW, happened to be $1,100 million less than the continuing resolution stipulated

Even the politically sensitive cancer and heart and lung programmes did not escape the knife—they were given $59 million and $44 million, respectively, less than the continuing resolution would have provided And the rest of the institutes of NIH between them received some $123 million less than the amount available

Congress has thus been trying for several months to change the law to give itself a stronger grip on the purse-strings Last week, the House of Representatives passed a bill which would require the President to inform Congress if he intends to impound appropriated funds, and to release the funds if either the House of Representatives or the Senate directs him to do so within 60 days The Senate had previously passed a stronger measure which would require that the funds be released as a matter of course unless both houses of Congress approve the refusal to spend the money The differences between the two bills must be resolved by a conference committee, but President Nixon has already promised to veto whichever version finally emerges

EXECUTIVE SHUFFLE

Train Moves On

by our Washington Correspondent

SINCE the Watergate scandal began to engulf some top officials in the Administration earlier this year, there has been much shuffling of Mr Nixon's team Last week, it was the turn of Mr Russell E Train, who was moved from the chairmanship of the Council on Environmental Quality to become Administrator of the Environmental Protection Agency Train, who is completely untainted by the Watergate cesspool, replaces William D Ruckelshaus, who was moved in April to head the FBI for a short time following the resignation of L Patrick Gray Ruckelshaus was also given a new job last week—he is now Deputy Attorney General

Train's appointment to one of the hottest seats in the federal government has been greeted with some muted criticism from both sides—from environmentalists who fear that he will not be tough enough and from automobile manufacturers who fear the reverse For his own part, Train said last week that he is his "own man", and that he will pursue a "strong, vigorous, fair enforcement policy"

The criticism that greeted his appointment is a fair taste of things to come, for Train will head the EPA during a critical phase of its existence In virtually every area there are tough decisions to be made which Train acknowledged last week, "will test the commitment of the American public" to cleaning up the environment One area in which particularly painful choices must be made is air pollution—the EPA has recently been issuing plans to meet the standards prescribed by the Clean Air Act which call for stringent cutbacks in traffic in some urban areas and for expensive emissions control devices to be fitted to automobiles Mr Ruckelshaus used to say when he was Administrator of EPA that he was happy when his decisions were attacked from both sides and by that criterion, Train has started off on the right footing

NEWS AND VIEWS

Leukaemia Viruses: Human or Feline?

DURING a news conference at Los Angeles in 1971, Dr R J Huebner, of the US National Cancer Institute, announced the discovery of a C-type RNA virus in human tumour cells which, he said, represented a "light year" leap forward in the aetiology of human cancer The virus which elicited the news conference was named RD-114, and details of its properties were subsequently published by McAllister *et al* (*Nature new Biol*, **235**, 3 , 1972) RD-114 virus was isolated from a human rhabdomyosarcoma cell line which had been inoculated into the brain of a foetal cat, and from the beginning debate centred on whether RD-114 virus originated from the human sarcoma cells or from the foetal cat in which these cells were grown The human origin was favoured because the internal proteins of the virus (group specific antigens and reverse transcriptase) were not immunologically related to those of previously described feline leukaemia viruses, and because the virus propagated could grow in human cells though not in feline cells On the other hand, attempts to isolate similar viruses from subcultures of the same human sarcoma cell line which had not been passed through cats were unsuccessful, and no evidence of a viral genome related to RD-114 was found in these cells using molecular hybridization techniques Neither did RD-114 virus seem to be related to the C-type viruses isolated from monkeys and apes

Recently, the uncertain origin of RD-114 virus has been resolved on the side of the cat In the May issue of *Virology* (**53**, 142 , 1973), Livingston and Todaro describe the isolation from feline cells of a virus that is indistinguishable from RD-114 virus The virus was spontaneously produced both by the CCC line of feline kidney fibroblasts and by other sublines of CCC cells which did not spontaneously release virus Even normal feline embryo cells could be induced to produce the virus after treatment with 5-iododeoxyuridine Thus RD-114 probably represents a latent virus of cats, when activated, it replicates more readily in human or primate cells than in CCC cells In this respect RD-114 virus of cats resembles the endogenous viral genomes of chickens and mice These viruses are known to be transmitted from one generation to the next as a set of "host genes", and they too are activated by 5-iododeoxyuridine to release infectious virus. Once activated, the chicken virus, like RD-114, replicates better in cells of other species

Livingston and Todaro's discovery of an endogenous cat virus resembling RD-114 is supported by similar biological studies from Sarma's laboratory (*Nature new Biol*, **244**, 56, 1973), and by a highly reiterated sequence of molecular hybridization studies (*Proc natn Acad Sci*, *USA*, **70**, 1437, 1973, and *Nature new Biol*, **244**, 51, 1973) from which Neiman's stands out for its clarity and lack of bombast All these papers show that feline cells, but not human cells, contain nucleic acid sequences that are homologous to the RNA of RD-114 virus The only remaining question on RD-114 is why several million dollars have been devoted to this particular virus Each of these seven recent papers, independently demonstrating the feline origin of RD-114, was supported by the US National Cancer Institute, all but one of them under contracts issued with the Special Virus Cancer Program (SVCP) But, it must be asked, whether the SVCP represents a better method of financing research than the traditional method based on peer review

No doubt laboratories sustained by SVCP contracts will now turn to other "candidate" human tumour viruses and they might do worse than examine a modestly presented but convincing paper published last year (in English) by a Soviet group of scientists (Zhdanov *et al*, *Arch ges. Virusforsch*, **39**, 309 , 1972), which describes a C-type RNA virus isolated from a human leukaemia cell line It is likely, however, that even when a virus is implicated in human leukaemia, it will be present in a latent form A possible lead in the detection of latent virus is the report by Todaro and Gallo in last week's *Nature* (**244**, 206 , 1973) that myeloblastic cells from a human patient with acute myeloblastic leukaemia have a reverse transcriptase possessing biochemical and antigenic properties closely similar to those of the enzyme of a C-type RNA virus isolated from an ape

Whereas RD-114 virus is probably inherited, two reports by Jarrett *et al* in the current issue of *J natn Canc Inst* and by Hardy *et al* (*Nature*, **244**, 266 , 1973) show that the ordinary feline leukaemia viruses (FeLV) are transmitted by "horizontal" infection Indeed, even cats that are first exposed to infection as adults have a high chance of developing leukaemia and possibly other diseases Thus leukaemia in cats is an infectious disease Because FeLV infects human cells in culture, there is the possibility that the human population may be exposed to infection This may also be true of RD-114 virus A leukaemia virus that is transmitted genetically in one host strain or species may be transmitted by infection to another. The host carrying the integral viral genome could act as a reservoir hidden from the epidemiologist.

Hardy *et al* point out that because FeLV is transmitted horizontally in cats, it may be possible to vaccinate cats against FeLV-associated diseases by inoculation with attenuated strains of virus The potential of vaccination against infectiously transmitted neoplastic disease has been proved with the successful vaccines developed against Marek's disease in domestic fowl, which is caused by a highly contagious herpes virus It is generally assumed that no protection could be developed against leukaemia caused by "vertically" transmitted viruses because the virus is already established in the cells of the host It is necessary to distinguish two fundamentally different modes of "vertical" transmission inheritance of DNA proviruses integrated in the chromosomes of the gametes, and congenital transmission of infectious virus particles In the latter case, one could envisage protection by maternal antibodies or by drugs which prevent the establishment of infection, for example inhibitors of reverse transcriptase There is also evidence that immunological tolerance is not the inevitable consequence of genetic transmission

From a Correspondent

PREDATION

Unpalatable Legumes

from our Plant Ecology Correspondent

MANY species of plant and animal have responded to intense predation pressure by developing toxic metabolites which render them unpalatable The development in plant seeds of insecticidal compounds has highly selective value for ensuring survival and ultimate germination A biochemical survey of various legume seeds, some of which are conspicuously free from insect predation, has now been carried out by Rehr, Bell, Janzen and Feeny (*Biochem Systematics*, **1**, 63, 1973)

In Central America and the southern United States, where the survey took place, legume seeds suffer attacks from a variety of Lepidoptera larvae and also from Coleoptera of the family Brucidae One abundant lepidopteran is the southern armyworm, *Prodenia eridania*, a polyphagous species which is known to be capable of consuming a wide variety of food plants, including many containing insecticidal toxins These toxins are apparently detoxified by *Prodenia* Its catholic appetite makes the southern armyworm an ideal test organism for use in bioassays of seed toxicity and palatability

Rehr *et al.* ground a variety of legume seeds and offered them incorporated into an artificial diet to *Prodenia* larvae Many of the seeds which did not suffer severe predation in the field contained high concentrations of unusual amino acids, these were extracted and then fed to the armyworms This provided a means of identifying precisely the repellent compounds involved in seed protection

Seeds of some legume species, for example *Cassia grandis*, which are heavily preyed upon in the wild, were found to contain no uncommon free amino acids A diet containing ground *Cassia* seeds proved quite acceptable to the armyworms and produced negligible mortality It is worth noting that this species produces large quantities of seeds, which presumably compensated for losses by predation

Entada polystachya suffers moderate predation from insects in the field and the seeds of this species were found to contain an unidentified amino acid A 5% ground diet of this species caused some pupal deformity in *Prodenia*, in which ventral abdominal segments were soft Deformed pupae either died or produced adults incapable of copulation

Legume species which were observed to be fairly free from predation, for example *Gymnocladus dioicus* and *Albizia julibrissin*, contained high concentrations of unusual free amino acids, in these cases β-hydroxy-γ-methylglutamic acid and albizziine respectively. A 5% *Gymnocladus* seed diet caused heavy mortality among the armyworms They were strongly repelled by material containing 4% of β-hydroxy-γ-methylglutamic acid, which is the concentration found in *Gymnocladus* seeds Normal L-glutamic acid at this concentration was neither repellent nor harmful to *Prodenia* larvae

Evidently there is a highly selective advantage, in terms of seed survival, in the production and accumulation of certain amino acids The protective system is most highly developed and most effective in plants such as *Gymnocladus* where toxin concentration is sufficiently high to be repellent to the predator even before consumption

NEUROTOXINS

Receptor Function

from our Neurochemistry Correspondent

NATURALLY-OCCURRING toxins continue to be fashionable and powerful weapons in the armoury of molecular pharmacologists bent upon the analysis of receptors and factors influencing their formation and function

α-Bungarotoxin has recently been used to "label" cholinergic receptors in cultured neurones from chick embryo sympathetic ganglia (Greene, Sytkowski, Vogel and Nirenberg, *Nature*, **243**, 163 , 1973) But the use of another toxin, histrionicotoxin, derived from a Colombian arrow-poison frog, has suggested that α-bungarotoxin may bind to a second site at the synapse in addition to the cholinergic receptor itself (Albuquerque, Barnard, Chiu, Lapa, Dolly, Jansson, Daly and Witkop, *Proc. natn Acad Sci U S A*, **70**, 949, 1973)

The excitatory action of acetylcholine (ACh) at receptors on skeletal muscle involves two stages first, combination with receptor sites, followed by an increase in the permeability of the postsynaptic membrane to sodium and potassium ions, resulting in a transient depolarization As yet little is known about the increase in ion conductance, and how this is triggered by combination of ACh with its receptors Albuquerque *et al.* now report, however, that the perhydro derivative of histrionicotoxin reversibly blocks ACh-induced potential changed at endplates in normal muscles as well as at extrajunctional sites in chronically denervated muscles, apparently by preventing the potassium conductance change, and, to a lesser extent, the sodium conductance change Moreover, during successive ACh applications, the toxin becomes completely ineffective only after the first contact with ACh, suggesting that its action is dependent on an initial binding of ACh [illegible] the receptor Thus, H_{12}-histrionicotoxin may be extremely valuable in the investigation of the "ionophore", although the ideal "label" would be an irreversible binding agent

α-Bungarotoxin has previously been thought to affect neuromuscular transmission more or less irreversibly But Albuquerque *et al* report a partial recovery of the endplate potential after washout of α-bungarotoxin from poisoned diaphragm endplates These results together with results from binding studies using a tritium-labelled derivative of α-bungarotoxin indicate two classes of binding sites, one occupied preferentially by curare, at which α-bungarotoxin binds irreversibly, and the other occupied preferentially by histrionicotoxin, at which the binding of α-bungarotoxin is reversible Both sites are involved in synaptic excitation by ACh, and are equated by the authors with, respectively, the receptor site and the "ionophore"

More recently, Giacobini, Filogamo, Weber, Boquet and Changeux (*Proc natn Acad Sci U S A*, **70**, 1708, 1973) report how receptor blockade with a toxin from cobra venom affects the development of neuromuscular contacts in embryonic chick muscles In their system toxin binding is confirmed to be specific for the ACh receptor site by its almost complete abolition by a variety of known cholinergic ligands Chick embryos survive high doses of toxin and are therefore convenient for the study of the development of innervated muscle in the presence of toxin In normal conditions the development of the motor innervation takes place in three main stages First, from the fourth to the sixth day of incubation, motor nerve fibres invade the limb-bud muscles, and the first myotubes appear, with a diffuse localization of acetylcholinesterase From the sixth to the twelfth day a massive formation of myotubes occurs, and acetylcholinesterase becomes restricted to the myotendon junctions Finally, from the twelfth day onwards, muscle fibres replace the myotubes, and the nerve endings differentiate into motor endplates with a selective localization of acetylcholinesterase, at this stage action potentials can be seen, and the ACh sensitivity becomes restricted to the endplate region Embryos injected with toxin were found to become atrophic with a marked reduction in the growth and differentiation of skeletal muscles—in 16-d embryos which had been treated with toxin on the 3rd, 8th and 12th day, the majority of contractile elements were still present as myotubes Moreover, very few motor endplates could be seen, and the sciatic nerve, spinal roots and sensory ganglia appeared atrophic It is unlikely that the toxin affects impulse propagation, so these changes must be due to the lack of postsynaptic activation and hence of muscle contraction in the presence of toxin

The fact that postsynaptic blockade causes degenerative changes presynaptically suggests that there is some transfer of information between the muscle cell and the nerve terminal during development The authors rule out the possibility that this occurs *via* the neural feedback loop involving the sensory fibres from the muscle to the motoneurone by showing that in the extrinsic ocular muscles, which receive a purely motor innervation, toxin treatment still causes a reduction in the size of both the muscles themselves and the corresponding nerves

The results suggest that information is passed directly from the postsynaptic to the presynaptic cell in the opposite direction to the transmission of impulses Similar retrograde transsynaptic effects have been reported to take place in the brain after lesioning of particular areas (Cragg, *Brain Res*, **23**, 1, 1970), and also in the cervical sympathetic ganglion, in which *in vivo* treatment with 6-OH-dopamine, which selectively destroys the postganglionic adrenergic neurones, results in a marked decrease not only of tyrosine hydroxylase, but also of the preganglionically-located choline acetyltransferase (Black, Hendry and Iversen, *Brain Res*, **34**, 229, 1971)

ECOLOGY

Cycling and Degradation

THE cycling of materials in ecosystems, with particular reference to chemicals and mineral wastes which may cause environmental deterioration, was the subject of the British Ecological Society's symposium held at Leeds University, July 10–12, 1973 Dr M J Chadwick (York University) discussed the significance of biogeochemical cycles in disturbed environments and illustrated the principles involved in the recycling of polluted river water through heathland and the nitrogen balance sheet of a colliery spoil In the context of arable ecosystems, Dr R G Potts and G P Vickerman (Game Conservancy) suggested in their paper that although the quantity and diversity of pesticides used on farmland continue to increase the ecological hazards were hard to identify and long term agricultural benefits were intangible Causes of the reduction in the partridge population of 25 acres of downland were analysed and the biological significance of stability, diversity and predation in farmland ecosystems was discussed with reference to cereal aphids Dr F Moriarty (Monks Wood) reviewed the rate of release and subsequent dispersal of DDT showing that the proportion of DDT found in living organisms is minute and that amounts probably depend on the physiology of each species rather than on its position in the food web

In a paper by Dr A. Jernelov (WHO, Copenhagen) the global cycling of mercury using deposition data from the Greenland ice cap to monitor mercury contamination was critically examined Although industrial emission into the atmosphere has increased the quantity of mercury in the environment, he suggested that changes in agricultural practices which stimulate microbiological activity in the soil increase the rate of methylation of mercury, and its subsequent volatilization could explain higher mercury contents in organisms without any increase in the total amount of mercury in the cycle The nitrogen balance sheet in aquatic ecosystems was discussed by Professor W D P Stewart (Dundee University) Using the scanning electron microscope to identify structural granules and polyphosphate bodies in algal cells, it was possible to assay the nitrogen and phosphorus status of the water A substantial loss of nitrogen from the system was attributed to denitrification and low standing crops of algae to high levels of secondary production

Contamination of the atmosphere with radioactive debris from nuclear explosions at various times and places and to various altitudes, and its redeposition, has been studied by Dr D H Peirson (AERE, Harwell) who in his paper explained on a meteorological basis the passage of material from the troposphere, or from the stratosphere through the troposphere, down to Earth Dr A D Christie (Ontario University) followed with a paper on "Residence Times in the Atmosphere" Models used to interpret trace constituent distributions were critically evaluated

Seventeen papers covered various aspects of air, water and land degradation The use of biological surveys to detect pollutants by establishing biological patterns was critically examined by Professor R W Edwards and M W Read (UWIST, Cardiff) and in other papers methods of detecting pollution of air and water by non-ferrous metals were described Interactions between pollutants complicated the interpretation of their possible biological effects and in discussion the need for thorough "ecotoxicological" studies was stressed to determine what levels of pollution mean in biological terms

Factors inhibiting the recolonization by plants of colliery spoil, molybdenum tailings, uranium strip mined areas, pulverized fuel ash, kaolin clay spoil and chromate smelter waste were reviewed by American and British workers Nitrogen deficiency was a common feature in all these wastes but with adverse *p*H, specific ion toxicity and physical structure complicating revegetation procedure Dr S J Wainwright (University of Wales) and Professor H W Woolhouse (Leeds University) explained how the complex mechanisms of metal tolerance in grasses involved a number of metabolic systems Dr F T Carrucio (South Carolina) in a paper dealing with production of acidity in coal mine refuse showed how only one of four types of iron pyrite generated acidity and in conjunction with *p*H of ground water prior to mining activity could be used to predict potential acidity of spoil and plan remedial action during the mining operation

The concluding session on "Planning for Resource Renewal" opened with a paper by Dr R Curnow (Sussex University) which criticized many of the assumptions used in the MIT work on finite limits to growth Papers by Dr G Petsch (Ruhr Regional Planning Authority, Essen), C V R Tandy (Land Use Consultants) and M F Downing and Professor B Hackett (Newcastle-upon-Tyne) gave examples of rehabilitation of derelict landscapes and N Jones and W R Howells (SW Wales River Authority) examined the role of natural agencies, remedial work and a hydro-electric scheme in improving water quality of a river affected by metalliferous wastes

This symposium brought together a variety of experts involved in the scientific study of degraded environments The published papers will provide specialist workers in this field and all who are interested in environmental quality with much factual material which would otherwise be less readily accessible

POLYPEPTIDES

Aaargh!

from our Molecular Biology Correspondent

CALCULATING biopolymer conformations *ab initio* is not necessarily a reprehensible pastime so long as, to quote a legal view of a different vice, one does not do it in the street and frighten the horses All the same, when the predictions are not readily testable they are scarcely relevant, if the answer is already known they are not very interesting, whereas if it is not known but experimentally accessible, the prudent man will generally prefer to wait and see, and perhaps not reflect overmuch on whether the theoreticians had spoken sooth, or merely registered a gallant near-miss Whereas, from the very outset, calculations, even of a quite primitive nature, tended to yield satisfactory answers for the permissible combinations of backbone torsional angles that are available to a polymer chain, that is to say in some wise supplanted model building as a means of restricting the stereochemical choice, the evaluation of the energies associated with different geometries remains, not surprisingly, an altogether more doubtful proposition The class of homopolypeptides should offer by far the best hope of success, but the record in regard to experimentally defined systems is for the most part dispiriting An interesting example relates to a new but hypothetical helix, first posited by Tiffany and Krimm on grounds of optical properties of charged polypeptides in water This issue has stirred up the polypeptide field, not only because the discovery of a new, so to speak canonical, structure, where there was thought to be a random coil, would be a matter of some importance, but additionally because it bears on the thermodynamics and mechanism of protein denaturization and folding, and also on the appropriate standards to use for analysing the optical characteristics of proteins

The circular dichroism of fully ionized polylysine and polyglutamic acid, which because of their solubility in water have been adopted as reference compounds for unstructured parts of proteins, shows a prominent positive feature at about 215 nm, which can be suppressed in high concentrations of some salts, giving place to what Tiffany and Krimm inferred to be the genuine random coil spectrum The band at 215 nm they identified with a supposed extended state, which they equated with the left-handed 3_1 helix, characteristic of polyproline II This contention they later supported with conformational calculations, based on the intramolecular coulombic interactions of the ionized groups Subsequently, more elaborate calculations, taking into account the entire gamut of (in principle) calculable interactions, led another group of workers to reiterate the conclusion that the extended helix is indeed the preferred structure It had meanwhile been pointed out that the circular dichroism of the charged polypeptides in water and dilute salt solutions could be perfectly simulated by introducing an admixture of α-helix into the random coil (the polymer being of course fully α-helical in the unionized state) These two opposing views have led to a veritable ping-pong match in the literature, and Rippon and Hiltner (*Macromolecules*, **6**, 282, 1973) have weighed in with some data on sequential polymers with glutamic acid in the repeating unit, together with alanine or alanine and glycine These give qualitatively the same circular dichroism, with the same response to salt as charged monopolymers Heating induces a shift in the same direction as salt This is interpreted again in terms of an extended helix that melts to a true random coil Calculations, the authors aver, also throw up the 3_1 helix as the most stable form

Tiffany and Krimm (*Biopolymers*, **12**, 575, 1973) have now, however, started another hare the denaturants urea and guanidine hydrochloride accentuate the positive band in the circular dichroism of the charged polymers, and generate a somewhat similar effect in denatured proteins at low temperature They are undismayed by the consequences of their argument, namely that polypeptide chains in concentrated guanidine hydrochloride are not random coils but extended helices

At this point one must surely expect the sleeping dragon to wake and roar, but the protagonists of extended helices have anyway now been badly mauled by Miller and his colleagues on both experimental and theoretical grounds In the first place, Rao and Miller (*ibid*, 835) state that commercial samples of polyglutamic acid and polylysine are commonly incompletely deprotected, that is to say the esterifying groups which are present on the side chains during synthesis have not all been removed When Rao and Miller prepare polypeptides with a residuum of 5% or so of aromatic ester groups, the positive Cotton effect is clearly in evidence When the protecting groups are removed it vanishes completely It is hard to imagine that this will be the end of the story, and a riposte will be awaited with interest Rao and Miller then continue the demolition process by showing that whereas simple polyelectrolytes, as is well known, assume a stretched rigid conformation in the absence of supporting salts, the synthetic polypeptides, in which the charge sits at the end of a long side chain, undergo practically no such change, as judged by the relation between molecular weight and intrinsic viscosity In a second paper, Rai and Miller (*ibid*, 845) turn their attention to the calculations of conformation, and expose to view the frailty of the underlying assumptions There are doubts, for example, about the effective dielectric constant to use in computing the charge interaction, in where to place the point charge, and in how to distribute the counterions More, Rai and Miller note that the distribution of torsional angles along the backbone will depend

Revision of the Synaptic Circuit

For almost twenty years, the electrical model first described by Fatt and Katz (*J Physiol*, **115**, 320, 1951) has proved adequate to account for the action of a large number of substances on a great variety of chemosensitive membranes (Ginsborg, *Pharmacol Rev*, **19**, 289, 1967) In essence both excitation and inhibition are mediated by an increase in the conductance of a specific ion (or ions) through the neuronal membrane (Both direction and magnitude of the ionic flow are dependent on a specific ionic gradient across the membrane and the change in membrane potential and resistance, so the model was readily testable as the use of intracellular micro-electrode became established)

Perhaps Krnjevic and Schwartz (*Exp Brain Res*, **3**, 306, 1967) were the first to hint that synaptic transmission may involve other mechanisms when they reported that changes in membrane conductance were detectable during the depolarization of cortical neurones of the cat by acetylcholine (Krnjevic, Pumain and Renaud, *J Physiol*, **215**, 247, 1971) Later Weight and Votova (*Science*, **170**, 755, 1970) were able to show rather more conclusively that the slow EPSP of frog sympathetic ganglia is mediated by a decrease in membrane resistance Unlike the classical EPSP described by the model, the slow EPSP was potentiated rather than decreased by the intracellular injection of depolarizing current Furthermore it was decreased by hyperpolarization and finally reversed in direction at a level close to that of the equilibrium potential for potassium They propose that the synaptically evoked excitation was the result of a decrease in the resting potassium conductance

In next week's *Nature New Biology*, a paper by Paupardintritsch and Gerschnseld is accompanied by two illustrations whose extremely elegant records show both excitatory and inhibitory potentials evoked by 5-hydroxytryptamine to be mediated by a decrease in membrane permeability Again the reversal levels are such as to suggest that the excitation is mediated by a decrease in the resting membrane permeability to potassium and inhibition due to decrease in the resting influx of sodium Less than a month ago Weight and Padjen (*Brain Res*, **55**, 219, 1973) confirmed that the slow IPSP of the sympathetic ganglia also behaves as if it were mediated by a decrease in sodium permeability They have likened this response to the hyperpolarization response of vertebrate photoreceptors to light (Baylor and Fourtes, *J Physiol*, **207**, 77, 1970, Tomica, *Q Rev Biophys*, **3**, 179, 1970), and drawn attention to the results of Engberg and Marshall (*Acta Physiol Scand*, **83**, 142, 1971) and Siggins *et al* (*Science*, **171**, 192, 1971) who attributed the inhibitory action of noradrenaline to an inactivation of the resting sodium conductance crucially on the degree of cooperativity of the conformational interconversion There is in fact no reason to anticipate cooperative behaviour as regards the melting of the extended helix, and calculation of interactions over increasing distances along the chain indicates that there should also be no local order Given that the conformational entropy does not actually favour an extended helical state over the coil, Rai and Miller conclude that all energetic factors that they can calculate should combine to produce a random coil with the charges at the ends of the side chains, the interactions of neighbouring residues appear actually to have the opposite effect on the coil dimensions to that in polyacrylate for instance

The circular dichroism is of course sensitive to conformation, and characteristic of the combination of torsional angles defining each well in the potential energy map To the extent that the distribution of segments between these wells in the random coil will depend on the nature of the side chain, so also will the nature of the circular dichroism. At this stage one would guess that the 3_1 helix will ultimately go the way of the dreaded 3_{10}, that comet of ten or so years ago, which caused such turmoil in the field, only to vanish quite abruptly and with the merest whimper

LIQUIDS

Molecular Motions

from a Correspondent

IN retrospect, the very successful meeting under this title organized by the Société de Chemie Physique at Orsay on July 2–6 could hardly have been better timed to take stock of this burgeoning field About 160 workers attended and some sixty papers were heard, experimental topics being drawn from virtually the whole range of optical, acoustic, dielectric and particle-scattering methods now available for liquid studies A limited number of purely theoretical papers were given, backed up by the latest in molecular dynamics calculations, the influence of which could be detected throughout most of the programme

The meeting began in somewhat austere fashion, Professor J Yvon (University of Paris) warning the participants with a certain *froideur* that classical liquids were non-existent, that they had better not forget that all the interactions they were concerned with were electromagnetic in character, that pressure is not quite the simple variable it seems to be and that, were it not for the Pauli exclusion principle, all liquids would be, at most, statistically neutral The extent to which these admonitions were taken to heart was not immediately evident in what followed

The focal point of the meeting was a set of "state of the art" lectures P Schofield (AERE, Harwell) on the theory of transport phenomena, J Lamb (University of Glasgow) on ultrasonic relaxation, C Brot (University of Nice) on correlation functions and orientational motion, S Bratos (University of Paris) on vibrational motion in liquids, H G Hertz (University of Karlsruhe) on NMR applications, T Springer (University of Julich) on neutron spectroscopy and P Lallemand (University of Paris) on light scattering

In these lectures and the many related shorter communications certain themes recurred constantly and served to define the interpretive limitations which can still frustrate even the most spectacular advances in experimental technique As expected, rotational motion dominated discussions, with emphasis on the newer results from infrared linewidths, depolarized Raman and Rayleigh–Brillouin scattering One was conscious throughout of the still-expanding legacy of Gordon's 1968 paper on the extraction of rotational information from infrared linewidth measurements which could be said to have inspired perhaps as many as a quarter of the papers presented

As the contributions of Brot and Bratos succinctly demonstrated, the extraction of autocorrelation functions, now available independently for the first three spherical harmonics (dielectric, magnetic dipole or electric quadrupole and light scattering respectively), is reasonably well understood, though, even in favourable cases where a successful deconvolution of coupled processes is possible, the molecular information remains severely under-determined and many open questions remain Brot cautioned against excessive reliance on either the Debye diffusion or the jump-diffusion models and urged that mechanistic conclusions be drawn with care, even when autocorrelation is clearly exponential

It was perhaps the complete dominance of the language of autocorrelation and memory functions which distinguished this meeting from others with similar titles held several

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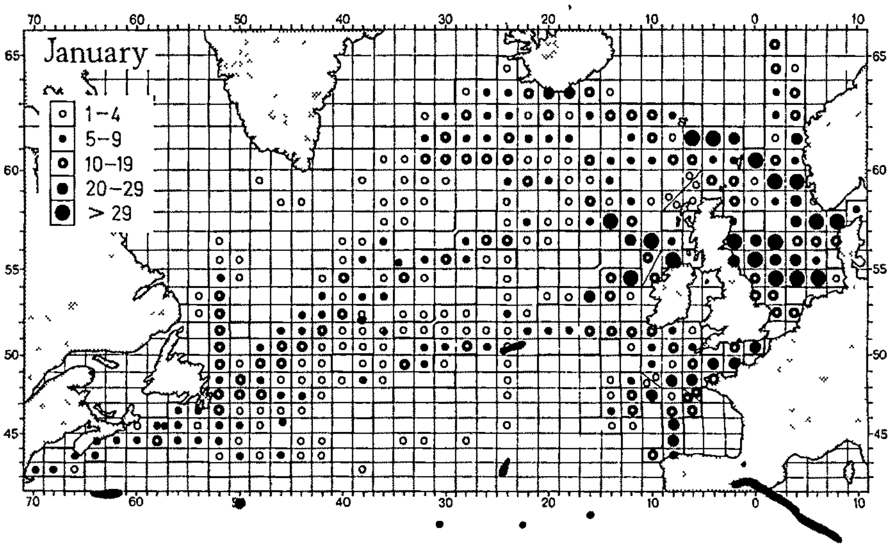
OCEANOGRAPHY

New Plankton Atlas

As a tribute to Sir Alister Hardy, who conceived and first developed the Continuous Plankton Recorder (CPR) in the early 1930s, the Edinburgh Oceanographic Laboratory (now part of the Institute for Marine Environmental Research and financed by the Natural Environment Research Council) has prepared a plankton atlas of the North Atlantic and North Sea (*Bull mar Ecol*, **7**, pp xix+174, 1973) which provides charts of distribution of 255 species or groups of planktonic organisms averaged from monthly samples during the period 1958 to 1968 The recorders were towed at a depth of 10 m once in each month along several standard routes

This map shows the number of analysed samples in the standard rectangles of 1° latitude × 2° longitude taken in each January during the survey period The numbers have been divided into five categories which are denoted by symbols (see key), the heavy lines delimit the sampled area Many of the charts demonstrate the close association of species with the principal current systems of the North Atlantic

At present, recorders are towed for more than 120,000 miles each year and by the end of 1971 ships of nine nations had towed the instruments for a total of 1,850,000 miles The Natural Environment Research Council, with the help of the United States Government, is now financing the design and development of a new Undulating Oceanographic Recorder which will measure and record physical variables as well as sample the plankton in the upper 75 or 100 m of the oceans



years ago Although occasional dissenting voices were raised (Mansel Davies (University College of Wales, Aberystwyth) making an impassioned plea for explanations in terms of "individual molecules and what they are doing") it was clear that the majority of authors were quite at home with autocorrelation functions, even though the temptation to see in them the more picturesque mechanisms of earlier times was clearly irresistible to some There was, in fact, a certain groundswell of reaction against the established physico-chemical vocabulary of "activation energies", "collisions" and "migrating defects" and a noticeable insistence on cooperative motions and coupling Translation-rotation coupling was frequently alluded to, though there appeared to be a certain confusion between simple statistical correlation and actual mechanical coupling—the latter being presumably a truism, given conservation of angular momentum

A regrettable consequence of the tight programme was that there was little opportunity to learn in detail about the newest experimental techniques Remarkable among the short contributions were the photon-correlation light-scattering work of Demoulin, Ostrowsky and Montrose (ENS and Catholic University, Washington), the use of low-frequency depolarized light scattering to obtain collective orientational correlation times by Gershon and Oppenheim (University of Beer Sheva), the measurement of anisotropy in rotational motions by J E Griffith (Bell Labs), the ingenious combination of results from NMR and neutron spectroscopy by M D Zeidler (University of Karlsruhe), the pressure-dependence of Rayleigh scattering by Dill and Litovitz (Catholic University, Washington) and the use of paramagnetic ESR probes for the study of liquid motions by Martini, Romanelli and Burlamacchi (University of Florence) If tentative conclusions can be drawn, they might be that the newer optical techniques have established an edge over those of NMR, conventional ultrasonics, dielectric dispersion because of their more favourable place in the time-scale of molecular processes except where special, chemically interesting systems are concerned

Nevertheless, optical methods did not have complete monopoly of experimental virtuosity A Mills (ANU, Canberra), for example, described how sense is at last being made of the conflicting data on self-diffusion coefficients, particularly for water Results to date indicate almost beyond doubt that the square-root law of mass-dependence does not apply to isotopic variants HDO and HTO

Dielectric measurements, though less conspicuous than in earlier times, continued to be described, though with a certain shift of emphasis towards non-dipolar liquids Mansel Davies discussed FIR absorptions in molecules such as CS_2, CH_4, benzene and so on, whereas dielectric absorption by n-alkanes in the range 26-140 GHz had been measured by U Stumper (University of Gottingen) On the theoretical side R H Cole (Brown University) outlined a new derivation of Glarum's formula for the dipole correlation functions from microscopic arguments which again challenged the alternative result of Fatuzzo and Mason

An afternoon was devoted to expositions of recent "molecular dynamics" calculations by two leading exponents, L Verlet (Orsay) and A Rahman (Argonne National Laboratory) Verlet's contribution concerned mainly simple liquids, for which a major result is the now indisputable long tail to the velocity autocorrelation function — believed, though still not demonstrated (except in two dimensions) to indicate hydrodynamic, vortex-like motions behind a moving atom The implications of this for the computation of transport coefficients were taken up by Schofield, while Brot offered the engaging possibility that a rotating molecule might "lose" memory of its immediate past, then regain it after a hydrodynamic delay If the microscopic behaviour of liquids is really as perverse as this there will be much scope for future meetings

A Rahman described a recent simulation of 216 molecules of water using an improved version of the Ben-Naim–Stillinger potential He and Stillinger interpret the results as offering little evidence either for phonon-like behaviour, or jump diffusion, or Gaussian self-correlation in the proton motion, and equally little support for collective behaviour in the form of clusters, non-bonded regions and the like

Though perhaps, in the end, exposing more gaps than it was able to fill in the connexion between theory and experiment, the meeting demonstrated overall the very considerable progress which has been made, not only in understanding but in defining what one might reasonably expect to understand of the microscopic physics of non-simple liquids

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Conductivity Anomalies by Partial Melting?

FROM their measurements of geomagnetic variation fields, Reitzel *et al* (*Geophys J*, **19**, 213, 1970) and Camfield *et al* (*Geophys J*, **22**, 201, 1971) recently demonstrated that there are large electrical conductivity anomalies (enhanced conductivity) in the depth range 50-400 km beneath the western United States Beneath the Basin and Range Province and under the Southern Rocky Mountains of Colorado, for example, conductivity in the upper mantle can vary by as much as a factor of 100 within conductive structures which include an elongated ridge on the surface of the conductive mantle and a combined step and ridge

But what causes such large conductivity highs? In next Monday's *Nature Physical Science* Chan and colleagues consider a possible origin for the anomalies which is suggested by the correlations with other geophysical phenomena Other workers have shown that the conductive structures beneath the western United States correlate strongly with, for example, heat flow and seismic wave velocity and absorption But, as Hales and Doyle (*Geophys J*, **13**, 403, 1967) have pointed out, regional variations in P wave and S wave velocity in the upper mantle can be explained most reasonably by a small amount of partial melting in the low velocity zone Is it possible, then, that partial melting can also account for the conductivity anomalies?

Chan and his colleagues thus examine this idea in the light of theories explaining electric conduction in molten silicate materials Specifically, they investigate the effect of 0 75–3 7% of partial melting on bulk conductivity in a situation where the melt has a much higher conductivity than the unmelted matrix It turns out that if 1% melting is to increase the bulk conductivity by a factor of 100, the conductivity of the melt must be about 10^4 times higher than that of the matrix, and so the problem is to find a mechanism which in, for example, olivine will increase the conductivity by such a factor on melting

After considering increases in ionic diffusion rates and intrinsic electronic conduction, Chan *et al* come down strongly in favour of a mechanism involving hopping between localized states of Fe^{3+} and Fe^{2+} (polaron hopping) because the conductivity of olivine is known to increase rapidly with increasing Fe^{3+}/Fe^{2+} ratio (oxidation) This is analogous to impurity conductivity in semiconductors at low doping concentrations On the other hand, the conductivity of the liquid melt should also be higher (but not by a factor of 10^4) because of a higher iron concentration there than in the matrix and the higher diffusion rate of Fe^{2+} with respect to Mg^{2+} Chan and his colleagues thus conclude that several mechanisms probably act together to account for the conductivity increase, but whatever these mechanisms are, a bulk conductivity increase by a factor of 10^2 because of partial melting seems quite feasible

HIGH ENERGY PHYSICS

Anti-proton Production

from a Correspondent

THE possibility of matter and antimatter co-existing inside a galaxy is suggested in some cosmological models such as that of Alfrén (*Rev mod Phys*, **37**, 652, 1965) The presence of a source region of antimatter somewhere in the Galaxy would be implied if an appreciable quantity of antimatter was to be detected in the primary cosmic ray flux Experiments reported to date have only been able to yield upper limits to the proportion of antiparticles ($\lesssim$0 1%) Indeed no one seems to have positively identified even one antinucleon reaching the vicinity of the Earth

Although 90% of cosmic ray particles are known to be protons many experiments concentrate on looking for antihelium and heavier antinuclei rather than antiprotons This is to avoid the problem of having to correct for the secondary flux of antiprotons produced in the collisions of primary cosmic rays with interstellar gas Experiments (for example looking for antihelium using superconducting magnetic spectrometers flown in balloons) therefore generally suffer from lack of a significant number of events (see, for example, Buffington *et al*, *Nature*, **236**, 335, 1972)

A considerable improvement in statistics could be achieved by measuring the antiproton to proton ratio, provided the contamination due to secondary effects can be accurately calculated Previous attempts at such calculations have suffered from the lack of sufficient information on the antiproton ($\bar{p}$) production cross-section ($p+\bar{p}\rightarrow p+$anything) Recently, however, T K Gaisser and R H Maurer (*Phys Rev Lett*, **30**, 1264, 1973) have used data now available on $\bar{p}$ production from the CERN intersecting storage rings (ISR) to calculate the expected $\bar{p}/p$ ratio due to collision effects Their results place a conservative upper limit of $\bar{p}/p \lesssim 4\,6\times10^{-4}$ arising from interstellar gas collisions at all energies

Drs Gaisser and Maurer have derived an expression for $\bar{p}$ production based on both conventional accelerator data and that from ISR Interpolation between these sets of data and extrapolation beyond ISR energies (>53 GeV in the centre of mass frame) are carried out on the basis of the scaling hypothesis of Feynmann

The $\bar{p}$ production inclusive cross-section is then used to calculate the expected $\bar{p}/p$ ratio Because the mean path length of matter traversed by primary protons between their source and observation at Earth (~3–5 g cm^{-2}) is much less than the interaction length for protons in hydrogen, the authors assume that each proton interacts at the most with one hydrogen nucleus, and also neglect further interactions of the produced antiprotons With the further assumptions that the primary cosmic ray flux in interstellar space is primarily protons with the same energy spectrum as observed in the vicinity of the Earth and that $\bar{n}$ production equals $\bar{p}$ production, an expression for the differential spectrum for antiprotons is derived. Feeding in a power low primary cosmic ray energy spectrum ($dN \propto KE^{-2\,6}dE$) yields the expected $\bar{p}/p$ as a function of antiproton energy.

Their calculations yield a $\bar{p}/p$ ratio initially increasing with energy but approaching an asymptotic limiting value of ~4 6×10^{-4} above ~100 GeV Drs Gaisser and Maurer emphasize that the result is very much a firm upper limit to the $\bar{p}/p$ ratio at all energies They argue that the final asymptotic figure is either insensitive to the approximations used or can only be reduced by more accurate treatment

The authors' conclusions do, however, seem to depend on the correctness of the scaling hypothesis Most recent ISR work and data from cosmic ray workers have raised considerable doubts concerning the applicability of scaling Thus there is an obvious need now to improve the experimental results to below the current upper limit of ~10^{-3} for the $\bar{p}/p$ ratio Sorting out such a small proportion of antiprotons from protons, however, is a formidable task.

LOW TEMPERATURE PHYSICS

Another Sound

from our Condensed Matter Correspondent

A COMPLETELY new type of sound wave may exist in liquid helium-four above its superfluid transition temperature, T_λ, according to a calculation by D C Mattis and L F Landovitz of Yeshiva University, New York (*Phys Rev Lett*, **30**, 1196, 1973)

The properties of liquid helium at temperatures above and below T_λ are so completely different that the two phases are distinguished by referring to them as He I and He II respectively Most of the research effort has been directed towards reaching an understanding of He II whose superfluidity and other "anomalous" properties have made it a substance of intense fascination for both theoretical and experimental physicists In comparison, He I has hitherto been regarded as relatively uninteresting, because its behaviour has seemed very similar to that of a dense classical gas

It has long been known that in He II there are two entirely different modes of wave propagation, referred to as first and second sound, and travelling with very different velocities First sound is characterized by density fluctuations as in "ordinary" sound and by the superfluid and normal component of the liquid moving in phase with each other, whereas in second sound the two components move in antiphase, so that the net density remains constant Because the proportion of superfluid falls to zero at T_λ, it has always been tacitly assumed that the only form of wave propagation in He II must be ordinary sound Experiments have shown that, as expected, the velocity of sound in He I is not greatly different from that of first sound in He II, and that it can be measured continuously through the transition, but that the velocity of second sound falls rapidly to zero as the temperature rises to T_λ

Mattis and Landovitz have now carried out a theoretical investigation of He I by considering collective excitations of the system, that is those involving the correlated motion of large numbers of atoms Their calculation shows that, at temperatures above T_λ, there should be, in addition to ordinary sound, another much more slowly propagating wave

For temperatures close to T_λ this wave should have the novel (for He I) character of being transverse, that is, the atomic motion being at right angles to the direction of propagation With increasing temperature, however, the velocity of the wave rises and the character of the disturbance gradually becomes less well defined until, eventually, at a critical temperature T_b, the wave becomes indistinguishable from ordinary (longitudinal) sound For temperatures above T_b the equations do not yield a wave solution The authors suggest that T_b probably corresponds to the boiling point In support of this thesis they report that the heat capacity, calculated on the basis of the same model, displays a "bump" at T_b, and they believe that, if account could be taken of the weakly attractive interatomic forces, a latent heat would then be found, characteristic of the phase change from liquid to vapour

Another interesting feature of their calculation is that, as the temperature falls, the velocity of the new wave drops to zero at T_λ The fact that, in He II, the velocity of second sound also falls to zero but as the temperature rises to T_λ suggests that, in some sense, the new sound wave represents a continuation of the second sound mode of the He II, into He I

The theoretical approach suggested by these authors may, perhaps, have laid the foundations for a new unified theory of both He I and He II The most encouraging demonstration of the general validity of their ideas would be an experimental observation of the new wave-mode which they have predicted in this paper

Ancient Linkage Groups and Frozen Accidents

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Evidence is presented that the genetic differences between man and the other mammals are extremely small. This supports the concept that natural selection conserves the *status quo*. The idea of evolution viewed as a succession of "frozen accidents" is discussed, taking as an example the remarkable similarity of the X-linkage group in all mammals both placental and marsupial.

No one would argue that the central concept of biology which congeals divergent disciplines into one cohesive whole is the Darwinian concept of evolution Evolution, in turn, is contingent on natural selection It is then of the utmost importance that we do not misunderstand the nature of natural selection At first, natural selection was thought of as an omnipotent advocator of progressively adaptive changes Those who still hold such a view see evolution as a relatively fast process, all inclusive in nature and affecting the entire genome More recent amino acid sequence analyses of a large number of direct gene products, on the other hand, indicate that the true nature of natural selection is most often that of an avid conservative extolling the virtue of *status quo* Could it be that extensive adaptive radiation of mammals actually involved only a very small fraction of the functional gene loci, while the rest remained relatively unmolested? If so, the genetic difference that separates man from other beasts might be surprisingly small

Several years ago, my colleagues and I made two postulates on the genetic content of human chromosomes (1) As an evolutionary freeze must have been placed on the X chromosome of a common mammalian ancestor, any gene locus which is found to be X linked in man must automatically be X linked in all other mammalian species[1-3] (2) At the stage of fish or amphibian, a mammalian ancestor must have undergone at least one round of tetraploid evolution Consequently, a homologous relationship may still be found among pairs of apparently nonhomologous human chromosomes[4-6]

Since then, cytological as well as genetic evidence in favour of those two postulates has steadily accumulated Here I shall discuss the extremely conservative nature of natural selection and the concept of frozen accidents within the context of human evolution and human linkage groups

Man and Apes

Differences between man and apes are obvious to the naked eye, yet such differences need not have involved a large number of gene loci in adaptive changes Although man is said to be a naked ape[7], a full set of fur can apparently be restored to the human body by a single dominant mutation[5] At each polymorphic gene locus, natural selection can favour a certain genotype only by eliminating other alternative genotypes as unfit Accordingly, a population which is undergoing rapid adaptive changes has to pay a considerable price for each gene locus which is subjected to selection This is what Haldane apparently meant by the "cost of natural selection"[8] It follows, then, that successful adaptive changes cannot involve too large a number of gene loci, otherwise a population would be exterminated by natural selection while undergoing these changes Although polymorphism has been documented for about 33% of the human gene loci tested[9], the very fact that human populations are not in the slightest danger of extinction suggests that natural selection has been oblivious to these polymorphisms, polymorphic alleles most often representing functionally neutral mutations[10] It would not be surprising if most of the gene loci in the genome were not involved in adaptive radiation which separated man from apes Indeed, haemoglobin α as well as β chain amino acid sequence is identical between man and the chimpanzee, while the gorilla differs by one amino acid substitution at each of these two chains[11]

Evolutionary Rates

Inasmuch as a greater number of the sequenced peptide chains have undergone evolutionary changes at rates slower than that for haemoglobin chains, one would expect that at many gene loci there would be no detectable difference between man and apes Although *samesense* mutations cannot easily be detected by sequence analysis of peptide chains, the expected ratio between *missense* and *samesense* mutations is only 17 6 Expressing the rate of evolutionary changes in terms of accepted point mutations (PAM)/100 amino acid residues/100 million years (m y) (which is about the time for which mammals have existed on Earth) the value obtained for haemoglobin chains is 14, whereas lower values of 0 06 for histone IV, 3 for cytochrome c, 4 for insulin and 5 for trypsinogen have been obtained[11] Evolutionary conservatism is indeed evident at many of the gene loci

One might argue that natural selection in the past has elevated most of the gene loci of higher vertebrates to states of near functional perfection, and that this is the very reason we no longer see much evidence of adaptive changes in many gene loci of man and apes Indeed, so far as haemoglobin chains are concerned, the rate of evolutionary changes appears to have slowed down noticeably in higher primates[12] Yet such an argument is revealing only a part of the truth and merely restating the point which I made earlier that natural selection can play the role of advocator of adaptive changes only on a very small fraction of the functional gene loci in the genome One can easily argue that *Escherichia coli* or any other contemporary organism in its own way represents a state of near functional perfection

The rate at which an organism evolves is greatly influenced by its generation time, the longer the generation time, the slower the rate of evolution Man, with a generation time of 15 yr, has gone through only 330 generations in 5,000 yr, whereas the mouse with a generation of 2 months would have gone through 30,000 generations in a comparable time The observed evolutionary slowdown in higher primates may simply be the consequence of progressive prolongation of their generation time

The X-Linkage Group

"Frozen accident" is the term coined by Crick to explain the universality of codons[13] Codons on messenger RNAs owe their very existence to anticodons on transfer RNAs The triplet coding system as we know it need not represent an ideal solution for the translation of a nucleic acid base sequence to an amino acid sequence of a peptide chain Nevertheless, at the very beginning of life on Earth, there occurred a functional coupling between messenger RNAs and transfer RNAs based on a triplet codon–anticodon recognition Once this occurred, an immediate evolutionary freeze had to be placed on the system, for any subsequent change in the coding system would necessarily have made a mockery of all previous messages, thus resulting in extermination of any living form which dared to attempt a change.

In fact, evolution can easily be viewed as successions of frozen accidents An enzyme seldom functions alone Most often a number of enzymes are functionally coupled together to constitute one metabolic system Once a reasonably well-functioning system was established, any drastic change in the kinetic property of one enzyme, without concomitant adjustments in the kinetic properties of functionally coupled enzymes, would tend to be disastrous Mutations being rare and random events, the chance of two or more independent gene loci concomitantly sustaining mutually acceptable mutations is practically zero Hence, the reason for an evolutionary freeze of the entire system

This concept of frozen accident applies as well to the observed conservation by diverse mammalian species of the X linkage group *in toto* The unique dosage compensation mechanism for X-linked genes which relies on the functional inactivation of one or the other Xs in female somatic cells[14] seems to have evolved in an ancestor common to both placental and marsupial mammals Thus the mechanism must be nearly 100 m y old

The invention of this particular form of dosage compensation mechanism would have necessitated the conservation *in toto* of the original X chromosome in all the descendants of that common ancestor, for the only acceptable X-autosome translocation would be a terminal fusion between the whole X and an autosome which brings about the so-called XY_1Y_2/XX scheme of sex chromosome constitution All other forms of X-autosome translocations which fragment the original X to separate pieces would disturb the established dosage compensation mechanism, and, therefore, be eliminated by natural selection Indeed, the X chromosome of most mammalian species seemed to be of the same absolute size comprising about 5% of the genome Exceptionally large X chromosomes seen in certain species such as the golden hamster, *Mesocricetus auratus*, and the field vole, *Microtus agrestis*, were found to carry excessive baggage in the form of genetically empty, constitutive heterochromatin[1]

X Linking in Other Mammalian Species

Is any gene locus which is found to be X linked in man automatically X linked in all other mammalian species? The list of gene loci which were found to be X linked in more than one mammalian species was originally very slim[2,3] With the increased use of the electrophoretic technique as well as interspecific somatic cell hybrids for linkage analysis, however, the list has rapidly grown to a more convincing proportion, as shown in Table 1 One may now accept the postulate as the fact that the X chromosome of any mammalian species, regardless of whether it be placental or marsupial, is the exact or near exact genetic equivalent of the human X chromosome The X-linked genes listed in Table 1 have no direct connexion whatsoever with the act of sex determination It is merely an evolutionary accident that a chromosome which happened to carry those genes was selected to become the X chromosome in an ancestor of mammals and that the subsequent invention of the particular form of dosage compensation mechanism put an evolutionary freeze on the entire linkage group There seems to be no better example of a frozen accident in evolution than the mammalian X-linkage group

Table 1 X Linkage in More Than One Mammalian Species

Human X-linked genes	X linked in other mammals	References
Glucose-6-phosphate dehydrogenase (E C 1 1 1 49)	Horse, donkey	18, 30, 31
	Hare	32
	Mouse	33
	Kangaroo	34
Phosphoglycerate kinase (E C 2 7 2 3)	Horse	18
	Kangaroo	35
Hypoxanthine-guanine phosphoribosyltransferase (E C 2 4 2 8)	Horse	18
	Mouse	33
Phosphorylase kinase (E C 2 7 1 3)	Mouse	36
Antihaemophilic factor viii	Dog	37
Antihaemophilic factor ix	Dog	38
X_G erythrocyte antigen	Gibbon	39
Dominant hypophosphataemic rickets	Mouse	*
Anhidrotic ectodermal dysplasia	Cattle	40

Those which are found to be X linked in two or more non-human mammals are not included In order to avoid a larger reference list, those referring to X linkage of the above genes in man are omitted

* In the linkage map of the mouse Distributed by M C Green, Jackson Laboratory, Bar Harbor, Maine (1972)

Various new staining techniques permit the visualization of characteristic banding patterns on individual chromosomes It has been shown that when stained with quinacrine mustard[15], the human X chromosome shows three brightly fluorescent spots, one in the middle of the short arm and two on the long arm[16] Although the observation that the same banding pattern is seen in various primate X chromosomes is, by itself, not too surprising[17], it is of more interest to note that the same banding pattern is also observed on the horse X chromosome[18] (Fig 1b) It may be that even the original linear order of these X-linked genes was conserved to a remarkable degree during mammalian evolution, although the very fact that some X chromosomes, such as that of the mouse are acrocentrics reveals that pericentric inversions did occasionally occur

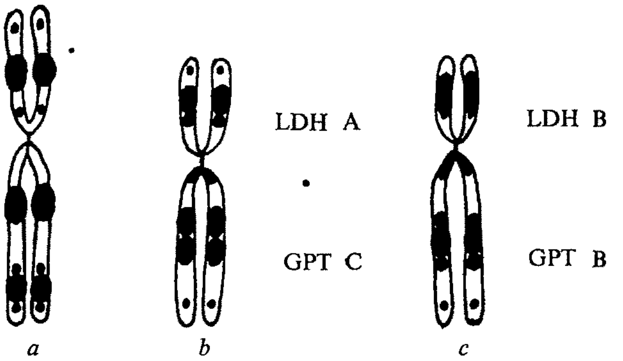

Fig. 1 *a*, Stylized quinacrine mustard banding pattern characteristic of the X chromosome of not only man and higher primates but also of the horse[17,18] Also shown is the stylized quinacrine mustard banding pattern of human chromosomes 11 (*b*) and 12 (*c*) In spite of a difference in the centromere location, the overall similarity in their banding patterns is quite striking

Homologous Relationship between Non-homologous Autosomes

So long as a particular function is assigned to a single gene locus in the genome, natural selection jealously conserves the active site of that gene product Thus, a trypsinogen gene would forever remain a trypsinogen gene, and a cytochrome c gene would remain a cytochrome c gene How, then, were successive additions to the genome of new gene loci with previously nonexistent functions made possible during vertebrate evolution? The mechanism of gene duplication provides a temporary escape from the relentless pressure of natural selection to a duplicated copy of a functional gene locus While being ignored by natural selection, a duplicated and thus redundant copy is free to accumulate all manner of randomly sustained mutations As a result, it may become a degenerate, nonsense DNA base sequence Occasionally, however, it may acquire a new active site sequence, therefore a new function and emerge triumphant as a new gene locus This new locus would again be placed under the protective shelter provided by natural selection, so that there would be no further accumulation of mutations which would surely lead to degeneracy

Gene duplication can be accomplished either by piecemeal tandem duplications involving one small chromosomal segment at a time, or in one fell swoop by tetraploidy Tandemly duplicated genes should form a closely linked cluster Indeed, in mammals, such a cluster is found with regard to haemoglobin β, γ, δ-chain genes as well as in genes for various classes of immunoglobulin heavy chains , γ, α, μ and so on Inasmuch as functional gene loci would comprise only a very small fraction of the genomic DNA[19-21], however, tandem duplications would more often result in the accumulation in the genome of nonfunctional DNA rather than in duplication of functional genes

Tetraploidy

Tetraploidy, on the other hand, duplicates every functional gene locus simultaneously, and the genes duplicated by tetraploidy should initially be unlinked from each other, although loose linkage may subsequently be established by chromosomal rearrangements The very fact that, in mammals, duplicated genes of more ancient origin are found unlinked from each other was the first clue which made us suspect that a mammalian ancestor might have gone through at least one round of tetraploid evolution at the stage of fish The genes for isozymic forms of various enzymes are often not linked to each other Similarly, the haemoglobin α-chain gene is not linked to the β, γ, δ-chain gene cluster, and immunoglobulin light-chain genes are not linked to the heavy-chain gene cluster

Tandem Repeats

The argument that all the duplicated genes of mammals originally arose as tandem repeats and that their non-linkage, if found, is merely the consequence of subsequent chromosomal rearrangements is unsound Tandem repeats form a very close cluster and the chance of an evolutionary compatible chromosome rearrangement breaking up such a tight linkage is as small as that of bringing together two originally unlinked duplicates to form a tight linkage

Indeed, tandem repeats seem to have stayed as tandem repeats throughout vertebrate evolution Close linkage of immunoglobulin heavy-chain genes has been observed on all three mammalian species in which sufficient genetic information has been obtained , man, mice and rabbits[5] Sexually mature testes of mammals as well as of birds contain a specific lactate dehydrogenase subunit , LDH C Thus a gene duplication which produced LDH C gene must have occurred before the ancestral vertebrate stock diverged into mammalian and avian lines Yet the genetic information available in certain avian species revealed persistent tight linkage between LDH B and C genes[22]

Fish and Amphibians

With the discovery of tetraploid and even octaploid bisexual frog species in South America[23], there was no longer a question that polyploid evolution was possible at the stage of fish and amphibians Furthermore, on trout and salmon which we consider tetraploid species on the verge of completing the process of diploidization, we found evidence of either doubling of the gene loci (four original homologues already differentiated into two separate pairs) or tetrasomic inheritance (four homologues still forming a quadrivalent in meiosis) with regard to almost all the enzymes and proteins which we and others studied[4,5] At this early stage following tetraploid evolution, only a few of the duplicated gene loci would have become silenced by sustaining function-depriving mutations It is not surprising then to find that trout and salmon appeared to have twice more gene loci for most enzymes even when compared with mammals

Chromosomal Changes

Regardless of what happened to the fish ancestor of mammals of 300 m y ago, at first glance it seems absurd even to entertain the notion that some of the original autosomal linkage groups of this ancestral tetraploid fish might have persisted in recognizable form all the way up to man, so that homologous relationships can still be found among certain pairs of nonhomologous human autosomes It is well to remember, however, that proteins and enzymes have changed only slightly during a comparable time

Of various types of chromosomal rearrangements, reciprocal translocations are the real culprits which break up the linkage groups Yet they are the very type which seldom accompany successful speciation, simply because heterozygotes for reciprocal translocations are, as a rule, semi-sterile A near sterile mating between semi-sterile heterozygotes does not often produce the translocation homozygotes necessary for the fixation of a reciprocal translocation as a species characteristic.

The most common chromosomal changes seen in vertebrate evolution are Robertsonian fusions which create one metacentric from two acrocentrics and inversions which, if pericentric in nature, change the position of a centromere Neither of these changes alone can drastically alter original linkage groups It is, then, not altogether unreasonable to expect that, in spite of apparently extensive chromosomal rearrangements which occurred since the time of a tetraploid ancestor, homoeologous relationships may still be found among certain pairs of mammalian autosomes in a haploid set

Chromosome Number

Although the diploid chromosome numbers of mammals range from a low of six to a high of eighty-four, the last census taken by Matthey in 1968 shows that more than half of the 668 species surveyed had numbers between forty and fifty-six, a peak being found at forty-eight[24] It may be that a common ancestor of mammals had forty-eight chromosomes If so, man and other higher primates might represent a group in which the ancestral chromosome complement was conserved with the least amount of chromosomal rearrangements

Based on banding patterns revealed by quinacrine mustard staining, Comings[25] was able to arrange twenty-two autosomes of man into eleven homoeologous pairs Only chromosome 18 was found to have no apparent partner Some of these resemblances between nonhomologues may be more apparent than real But a few are rather convincing One of these is a pair made of chromosomes 11 and 12 (Fig 1*b* and *c*) Furthermore, by the use of human–rodent somatic cell hybrids, it has been shown that these two chromosomes indeed harbour pairs of isozyme genes for lactate dehydrogenase (LDH)[26,27] and glutamic–pyruvic transaminase (GPT)[27], LDH A gene and GPT C gene are found on chromosome 11, whereas LDH B gene and GPT B gene are found on chromosome 12 The homoeologous relationship seems rather convincing on this pair of human autosomes My view is that in most instances homoeologous relationships will be found with regard to a small segment rather than along the entire length of two nonhomologues Using the method of *in situ* mRNA–DNA hybridization, Price *et al*[28] obtained suggestive evidence that the haemoglobin β, γ, δ chain gene cluster is carried by either chromosome 4 or 5, while the haemoglobin α-chain gene is on chromosome 2 Earlier linkage data, however, indicated that the β, γ, δ gene cluster is on chromosome 1 (ref 29) Chromosomes 1 and 2 were regarded as homoeologous by Comings[25] If the β, γ, δ gene complex is carried by chromosome 1 and the α gene by chromosome 2, at least a partial homoeologous relationship between these two largest autosomes of man may eventually be proven I find, however, a closer resemblance in the banding patterns on the long arms of chromosomes 2 and 4 The exact location of the haemoglobin β, γ, δ chain gene cluster is awaited with great interest

The idea that meaningful genetic difference which separates man from apes or for that matter man from the mouse or the horse is really very small might be quite disconcerting to some But such seems to be the nature of evolution dictated by natural selection which more often than not extols the virtue of *status quo*

Finally, it should be pointed out that when rapid evolutionary changes are encountered on certain genes, functional triviality of these genes rather than adaptive changes are indicated Of all the sequenced peptide chains, fibrinopeptides A and B show the fastest rate of evolutionary change, 60 PAM/100 amino acid residues/100 m y This rate is 1,000 times faster than that for histone IV (ref 11) These amino end peptides are discarded from fibrinogen during blood clot formation Their role being passive, most mutations do not affect the performance of their trivial function, hence, exceptionally rapid changes

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Absorber Theory of Radiation and the Future of the Universe

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The power input to a microwave source remained constant to 1 part in 10^8 as it alternately radiated into free space and into a local absorber. In the framework of the Wheeler-Feynman absorber theory of radiation, this result sets some constraints on possible future properties of the Universe.

THE existence of complete absorption of radiation along the future light cone is normally taken as a precondition for the application of the Wheeler-Feynman absorber theory[1,2] (but see ref 1, page 175, for a counter example) But as Davies has recently been at pains to point out[3], many Friedmann models are not opaque in the future In particular, all open, ever-expanding, cosmological models exhibit less than complete absorption along a future light cone If our Universe conforms to such a model, one might detect some of the advanced effects referred to in ref 1 In this article I report the results of a sensitive search for one such effect, a reduced power drain on a source radiating into an incomplete absorber

It is also possible to link the question of the absorptive properties of the Universe to the oft-debated question of the direction of time's arrow in closed cosmological models The direction of time may be separately specified by considering cosmology (expansion of the Universe), statistical mechanics (increase in entropy) or the emission of electromagnetic energy Are these three arrows of time related, and if so, how? This question is discussed at length by Gold[4,5], Gal-Or[6], and Cocke[7], who presents a model for "two-time statistical boundary conditions", suggesting a symmetrical reversal of time's arrow at the point of maximum expansion of the Universe

More recently, Davies[8] raised the issue again, and discussed in some detail an objection to simple models of the type suggested by Gold[5] and Cocke[7] One may understand the objection by considering a diverging beam of monochromatic radiation emitted into free space at time A, such as the present, in the expanding phase of a closed Universe (Fig 1) I assume that some of the radiation passes the epoch of maximum expansion and is absorbed (as far as we are concerned) at B, which need not be near the singularity, $R=0$ In a time reversed cosmology, an "observer" at B will interpret the event as an emission To produce absorption of the diverging beam originating at A, a very large number of sources at locations like B must spontaneously emit radiation of precisely the correct phase and frequency to produce a temporal mirror image of the signal emitted at A (my unpublished work with J A Wheeler) As Davies argues, this "accidental conspiracy" is unlikely If the "accidental conspiracy" does not occur in the time reversed model, then radiation emitted at A may not be fully absorbed

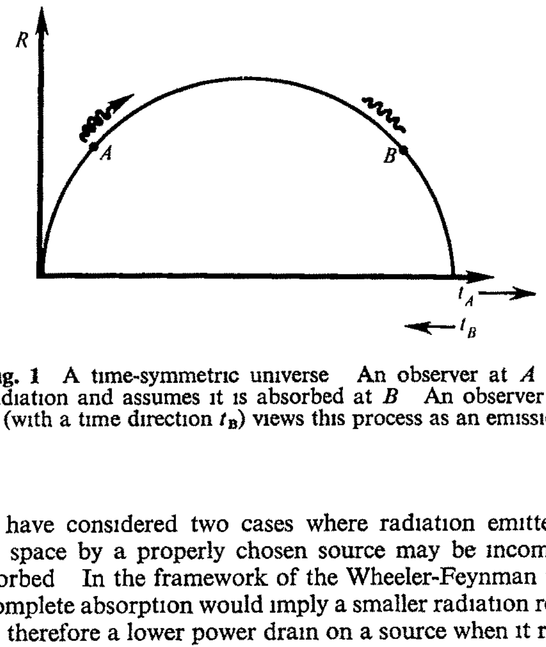

Fig. 1 A time-symmetric universe An observer at A emits radiation and assumes it is absorbed at B An observer at B (with a time direction t_B) views this process as an emission

I have considered two cases where radiation emitted into free space by a properly chosen source may be incompletely absorbed In the framework of the Wheeler-Feynman theory, incomplete absorption would imply a smaller radiation reaction and therefore a lower power drain on a source when it radiates into free space than when it radiates into a local (complete) absorber

$$P_f = (1-\delta)P_a \qquad (1)$$

Here P_f is the power input to a source when it radiates into free space and P_a is the power drain when it radiates into a total, local, absorber Ordinary experience dictates that δ must be small The aim of the experiment reported here was to set a direct upper limit on δ

Cosmological Absorption of Microwave Radiation

Can we transmit an electromagnetic signal which, if it is absorbed at all, will be absorbed only at very large distances, in the very distant future? The answer seems to be yes. I chose to work with microwaves because the absorbing properties of local matter at microwave frequencies are known to be small. The absorption of the Earth's atmosphere at $\lambda = 3$ cm is less than 3% at the zenith in clear weather. Absorption of 3 cm radiation by the Galaxy is negligible except at low galactic latitudes. In addition, the antenna used had a beam far larger than the angle subtended by the galactic plane. Hence, I can safely set galactic absorption $\leq 1\%$.

Intergalactic extinction of two types may occur. First, there may be a line absorption by neutral intergalactic hydrogen. As the 3 cm radiation propagates through an expanding Universe it will be redshifted. If the Universe continues to expand sufficiently, the wavelength of the radiation relative to the matter it traverses will reach 21 cm, so that it will be absorbed by neutral hydrogen. It is easy to show, however, that this absorption can be neglected. I make the extreme assumption that all the matter in the Universe is in the form of neutral hydrogen. Observed upper limits[9] on the deceleration parameter, $q_0 \leq 1.0$, imply that the present density of hydrogen is $\leq 3.5 \times 10^{-29}$ g cm^{-3} for $H_0 \leq 100$. At the epoch in the future when 3 cm radiation has been redshifted by a factor $z+1 \simeq 7$, the density of neutral hydrogen will be $\leq 10^{-31}$ g cm^{-3}. The work of Field[10] may be used to show that the 21 cm line absorption is less than 1.5×10^{-3}, where I have used the fact that the spin temperature T_s must be at least as large as the temperature of the microwave background at that epoch, $2.7\ (z+1)^{-1}$.

Table 1 Values of $\Delta I/I$, Determined from the Chart Recordings, for Four Phases of the Signal Relative to the Cosine Wave Driving the Ferrite Switch

Phase (φ)	Termination at AA'	No. of runs	$\Delta I/I$ ($\times 10^{7}$)
0°	Absorber	38	$+14.7 \pm 7.7$
90°	Absorber	26	-6.4 ± 7.4
180°	Absorber	40	-10.3 ± 7.7
270°	Absorber	24	-8.0 ± 8.8
0°	Antenna	14	-7.4 ± 7.7
180°	Antenna	17	0.0 ± 5.6

In each case, ΔI is the difference in the input current with the principal horn antenna uncovered and covered. $\Delta I = I_u - I_c$. Errors are standard deviations of the means.

Second, Thomson scattering from intergalactic electrons may occur[11]. The mean free path against scattering is very large, $\gtrsim cH_0^{-1}$, and in any case, scattering, unlike absorption, is a time-symmetric process.

I conclude that at least 95% of the microwave radiation leaving the antenna will reach cosmological distances before being absorbed (if it is ever absorbed[3,12]).

Experimental Details

The apparatus used in these observations is shown schematically in Fig. 2. Microwaves at 9.7 GHz were generated by a commercial impatt diode oscillator (Varian model VSX 9522P). The efficiency, ε, of this diode was about 4% at the voltage level used. The output of the oscillator was alternately switched between an absorptive termination and a large conical horn antenna (originally constructed by Roll and Wilkinson[13]). The switching element was a four-port ferrite switch driven at 1 kHz; the insertion loss at 9.7 GHz was a few tenths of a dB. During each cycle of the ferrite switch, the diode thus radiated alternately into a virtually complete "here and now" absorber and into the antenna which was pointed at the zenith. Had the radiation reaction caused by local, and by very distant, matter differed, the power inputs to the diode would have changed at the switching frequency and with a known phase. The power input to the microwave oscillator was monitored by measuring the current supplied to the impatt diode by a constant voltage power supply (Hewlett Packard model 6106A). Only the time varying (differential) power consumption is of interest. Therefore, a.c. preamplification and detection were used throughout.

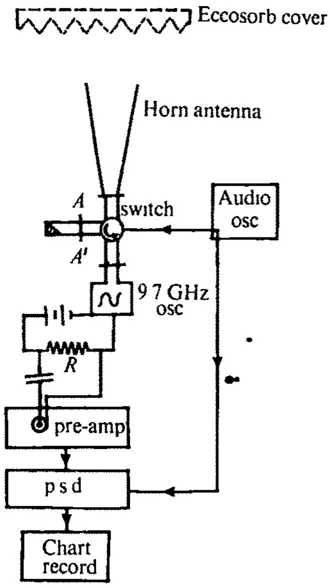

Fig. 2 Schematic of the apparatus. When in place, the eccosorb cover was actually 20λ above the opening of the antenna. For some observations, the absorptive termination at AA' was replaced by another small horn antenna radiating into free space.

Before phase sensitive detection, any 1 kHz voltage drop across resistor R was amplified 1,000 times by a low noise PAR model 113 preamplifier, with a 3 dB roll-off set at 300 and 3,000 Hz. Four phase settings were used on the phase sensitive detector: one with the signal input nominally in phase with the 1 kHz switching voltage, and others at 90°, 180° and 270° to it. The d.c. output of the phase sensitive detector was smoothed with a time constant of 1 s and recorded. Data were taken in 2 min blocks for each phase setting. Calibration of the phase sensitive detector was obtained by introducing a 1 kHz signal with known phase and voltage to its input.

To avoid systematic errors introduced by offsets in the phase sensitive detector and other electronics, alternate runs were made (1) with the antenna radiating freely into space, and (2) with the antenna radiating into a large absorbing sheet placed above the antenna. In the latter case, the output of the oscillator was at all times completely absorbed "here and now" for either position of the ferrite switch. Comparing runs with and without the local absorber above the antenna allows one to eliminate the systematic errors introduced by the electronics.

The absorbing cover was constructed of Emerson and Cuming CV-4 eccosorb, which has a reflexion coefficient less than -40 dB at 9.7 GHz. To ensure that near-field effects were minimized, the absorbing cover was placed twenty wavelengths above the antenna horn opening. Enough eccosorb was used to cover the antenna beam down to the -25 dB level in the E plane of the horn and to the -33 dB level in the *H* plane. Direct measurements of the antenna pattern[14] show that the absorption was 99% or more complete with the cover in place.

Five separate sets of observations were made, each including many runs with the antenna covered and many with the antenna uncovered. Clear, cloudless days and nights in August and September were chosen; runs were not made when the galactic plane lay near the zenith.

Finally, towards the end of the experiment, a further check on systematic error was made by replacing the absorptive termination at *AA′* (see Fig. 2) with a small horn antenna radiating freely into space. With an antenna on each side of the ferrite switch, the radiometer was thus balanced when the eccosorb cover was absent. In this configuration, runs were made with only two phase settings, 0° and 180°.

Results of the Experiments

The chart records provided values for ΔI, the difference in the current inputs with the antenna uncovered and covered. These values are tabulated below for each of the four phase settings employed. If δ is greater than 0 (see equation (1)), then $\Delta I/I$ should be negative for $\varphi=0°$ and positive for $\varphi=180°$.

Two additional steps are required to convert values for $\Delta I/I$ into a value (or upper limit) for δ. First, it is clear that ΔI will be proportional to the change in the power input only if the voltage across the impatt diode oscillator is constant. This was checked by monitoring the applied voltage directly; the proportional variation in the voltage at the switching frequency $\Delta V/V$ was always $\lesssim 4\times 10^{-11}$ which is less than the measured values of $\Delta I/I$, and may be neglected. Next, I must take into account the efficiency of the diode. If the total power consumption is P_c when the diode radiates into a local absorber,

$$P_c = P_h + \varepsilon P_c$$

where εP_c is the part of P_c actually emerging as microwave radiation and the remaining power (P_h) is dissipated as heat. The purpose of the experiment was to discover whether the power input to the diode changed when it was allowed to radiate into free space (antenna uncovered). I assume that only the part of the input power which actually emerges as microwaves is affected. Then

$$P_u = P_h + \varepsilon P_u = P_h + \varepsilon(1-\delta)P_c$$

and

$$\Delta P \equiv P_u - P_c = -\varepsilon\delta P_c$$

hence

$$\delta = -\Delta P/\varepsilon P_c = -\Delta I/\varepsilon I$$

where ε was experimentally determined to be $(3.8\pm0.2)\%$ during the observations.

Figure 3 is a plot of δ calculated in this fashion as a function of the phase setting, φ, of the detector. The effects predicted in the first section, with $\delta>0$, should have produced a cosine wave with a maximum at zero phase. A cosine curve was least-squares fit to the four points of Fig. 3, with the further restriction that it should have a maximum at $\varphi=0°$.

The result, and its associated standard deviation of the mean, is

$$\delta = (-1.1\pm1.6)\times 10^{-9} \tag{2}$$

A negative value of δ, if significant, would have implied that it "costs" more power to radiate into free space than into a complete, local, absorber. Even if we treat both phase and amplitude as free parameters in the fitting procedure, δ is clearly less than a few parts in 10^9.

The result is consistent with $\delta=0$, and thus conforms to ordinary expectations. It seems either that the analysis in terms of the Wheeler-Feynman absorber theory is incorrect or that absorption along the future light cone is complete to better than one part in 10^8.

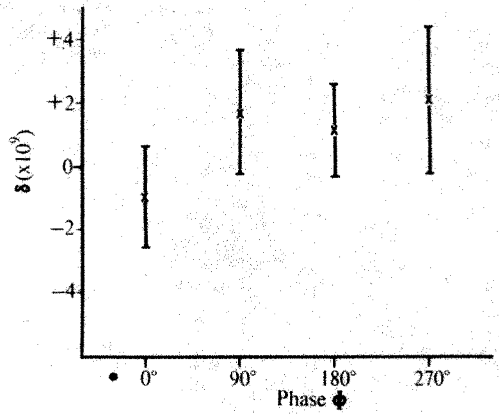

Fig. 3 The quantity δ as a function of the phase of the second detector. All runs have been combined, weighted by the inverses of the respective standard deviations of the means.

Finally, T. Gold (private communication) has pointed out that the existence of advanced effects, such as those searched for unsuccessfully here, might have vitiated the usual primaeval fireball explanation of the isotropic microwave background radiation.

Although the results of the experiment are not startling, like other null results (the Eötvös experiment[14,15] and the Hughes–Drever experiment[16,17]), they may prove useful to those investigating the general question of the interaction between local and cosmological physics.

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Horizontal Transmission of Feline Leukaemia Virus

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As feline leukaemia virus (FeLV) is shown to be transmitted horizontally it may be possible to vaccinate cats against lymphosarcoma and other FeLV-associated diseases.

MOST information on the spread of the leukaemogenic RNA viruses under laboratory and field conditions comes from the study of these viruses in the mouse and chicken. Vertical transmission (transmission of virus from parent to progeny through the gametes) is assumed to be the predominant route for the naturally occurring leukaemia viruses of the mouse[1,2]. Considerable evidence indicates that these viruses, in mice as well as fowl, are integrated in the host genome and are transmitted as Mendelian traits[3,4]. Horizontal transmission (viral spread by contact or contagion) is thought to play little or no part in the natural history of the murine leukaemia viruses. In fowl, however, contact infection has been convincingly demonstrated, showing that vertical and horizontal transmission need not be mutually exclusive[5].

The discovery of leukaemia virus in cats[6] and the development of serological methods[7-10] for identifying the feline leukaemia virus (FeLV) allow the determination of the relative importance of these two modes of transmission in animals other than mice and fowl. Serological studies have established that FeLV can be demonstrated in approximately 90% of cats with feline lymphosarcoma. In addition to lymphosarcoma, other feline diseases have shown a striking association with FeLV. These include myeloproliferative disorders, infectious peritonitis, fibrosarcomas, and certain non-responsive anaemias[7-9]. Furthermore, as in the mouse and chicken, clinically normal cats have been found to harbour FeLV[9].

Recent epidemiological studies on feline lymphosarcoma gave no evidence for horizontal transmission of FeLV[11-13] but cases of apparent contact infections with FeLV have been observed in laboratory cat colonies[14,15]. We have previously reported the occurrence of numerous household clusters of feline lymphosarcoma (two or more cases in cats from one household[7,9,16]). Most of the cluster cases occurred in unrelated cats, a fact that suggested horizontal transmission of FeLV, with subsequent development of lymphosarcoma. The use of a simple serological test for the detection of FeLV has now made possible the testing of a large population of clinically normal cats. Our findings indicate that horizontal transmission of FeLV is common and that cats naturally infected in this fashion have a high risk of developing lymphosarcoma.

Occurrence in Normal Cats

Peripheral blood smears from cats were tested for FeLV by indirect immunofluorescence using absorbed rabbit antiserum to FeLV group specific antigens[9]. Figure 1 illustrates the characteristic cytoplasmic fluorescence seen in the leukocytes and platelets of FeLV infected cats. Table 1 shows the results of parallel tests on specimens using three methods for FeLV detection ; the immunofluorescence on peripheral

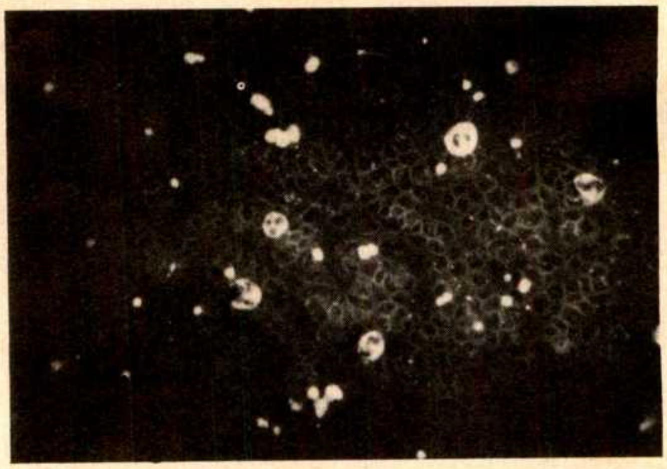

Fig. 1 Punctate granular cytoplasmic fluorescence representing FeLV gs antigen in peripheral blood leukocytes and platelets from a normal cat living in a household with a history of feline lymphosarcoma.

blood smears[9], the detection of FeLV group specific antigens by immunodiffusion[7] and the recovery of infectious FeLV in tissue culture[8]. The methods all gave similar results, indicating that demonstration of FeLV group specific antigens in peripheral blood cells by immunofluorescence identifies FeLV infected cats.

Thirty-eight household clusters of feline lymphosarcoma were studied (Table 2). One hundred and seventeen cats developed lymphosarcoma in the cluster households (average of 3.1 cats with lymphosarcoma per household), two-thirds of the cases occurring in unrelated (not parent, offspring or sibling) cats (Table 2).

Table 1 Comparison of FeLV Detection Methods

Diagnosis	Number of cats	FeLV status determined by Immunofluorescence	Immunodiffusion	Infectious FeLV isolated in tissue culture from Tumour	Plasma	Salivary gland	Urine
Lymphosarcoma	5	+	+	5	5	5	3
Normal	5	+	+	No tumour	5	5	2
Normal	5	–	–	No tumour	0	0	0

Tumour tissue and salivary glands were extracted as 20% homogenates in phosphate buffered saline. The extracts (clarified by centrifugation), undiluted plasma and undiluted urine were filtered through a 220 µm filter and 1 ml of the filtrate was added to freshly passaged cultures of feline embryo fibroblasts (FEF). FeLV infection was assayed by development of FeLV gs antigen (demonstrated by immunofluorescence[9]) in acetone fixed FEF cells or by isolating FeLV from culture media by density gradient centrifugation and demonstrating FeLV gs antigen by immunodiffusion[7].

Table 3 shows the results of immunofluorescence tests on the peripheral blood of 543 apparently normal cats from households with a history of cats with lymphosarcoma or other FeLV-associated diseases. 33% of these normal animals were infected with FeLV. Normal cats living in households already having two or more cats with lymphosarcoma were twice as likely to be infected with FeLV than those from households having only one cat with lymphosarcoma or cats with other FeLV-associated diseases.

Table 2 Kinship and FeLV Status of Cats with Lymphosarcoma from Cluster Households

Total number of clusters	Number of cats with lymphosarcoma Total	Unrelated cats	Related cats	FeLV status of cats with lymphosarcoma Number examined	FeLV+	FeLV+(%)
38	117	78	39	56*	51	91

Cluster household cats were considered related if lymphosarcoma developed in either parent and offspring, or two or more siblings. FeLV status was determined by immunofluorescent detection of FeLV gs antigen in leukocytes and platelets in peripheral blood smears.

* Only fifty-six of the 117 cats that developed lymphosarcoma were examined for FeLV. The remaining sixty-one cats died before the study began.

Table 4 summarizes our experience with immunofluorescence tests on 2,005 apparently normal cats, 543 living in households with a known history of an FeLV-associated disease and 1,462 living under other circumstances. Normal cats living with infected cats have a high risk of becoming infected. Overt FeLV infection in normal cats living under other circumstances is extremely rare. Thus only two of 1,462 (0.14%) normal cats from environments other than households with a history of FeLV-associated diseases were infected with FeLV.

FeLV-Related Disease in Carriers

What is the subsequent course of FeLV$^+$ normal cats? Do they have a heightened incidence of lymphosarcoma or other diseases? We have followed up 148 of the 177 FeLV$^+$ normal cats identified in our studies (Table 5). 16.2% have developed histologically confirmed lymphosarcoma and 7.5% of the cats have died of non-responsive anaemias with no histological evidence of lymphosarcoma. The average time elapsing between FeLV detection and lymphosarcoma development was 5.3 months, with a range of 1 to 24 months. The expected lymphosarcoma incidence in the general cat population for a 5.3 month period is 18.3 cases per 100,000 cats at risk[17], thus we would have expected 0.018 cases to have developed in these 148 cats. The observed incidence of lymphosarcoma in FeLV$^+$ normal cats was 888 times greater than the expected incidence.

The natural development of lymphosarcoma was followed radiographically in a normal cat shown to be infected with FeLV. Initial radiographs of the cat showed no evidence of lymphosarcoma (Fig. 2*a*). Three months later, radiographs of the thoracic cavity revealed a large lymphoid tumour mass of the anterior mediastinum (Fig. 2*b*).

A syndrome of FeLV-associated non-responsive anaemias in cats has been recognized and appears similar to the disease induced in Balb/c mice by certain strains of Rauscher leukaemia virus (ref. 18 and W. D. H., jun., unpublished). Epidemiologists looking only for lymphosarcoma as evidence for horizontal infection with FeLV have not included deaths due to anaemia in their data. If we combine the FeLV$^+$ normal cats that developed lymphosarcoma and those that developed non-responsive anaemias, then a total of 23.7% of all FeLV$^+$ normal cats developed an FeLV-related disease. In this connexion, many young cats die of an ill defined syndrome known as the "fading kitten syndrome". Recent experiments on kittens experimentally infected with FeLV have produced a very similar syndrome which is associated with thymic atrophy[9]. Thus, FeLV may be the aetiological agent for at least two, and possibly more, non-neoplastic diseases of cats.

FeLV Transmission

How is FeLV transmitted from cat to cat? Three routes should be considered: saliva, urine, and blood. FeLV was found in the parotid salivary glands of thirty-two FeLV$^+$ lymphosarcoma cats but was not found in salivary glands of six FeLV-lymphosarcoma cats nor in eleven normal FeLV$^-$ cats. Saliva may be the most likely vehicle for spreading FeLV as cats are social animals using their suitably bristly tongues for grooming themselves and companion cats. Aerosolization of FeLV through salivary and nasal secretions may play an important role in disseminating the virus. In support of this it may be noted that Rauscher murine leukaemia virus can be experimentally transmitted to Balb/c mice by exposure to aerosol virus[20].

FeLV group-specific antigen can be detected in the kidneys of 70% of cats with lymphosarcoma[8,9]. Antigen was present in the infiltrating neoplastic lymphocytes as well as in discrete deposits on the glomerular basement membranes. Infectious FeLV and neoplastic cells infected with FeLV can pass through damaged kidneys into the urine (Table 1). The signficance of this is evident when one considers the use of communal litter pans in urban households with several cats.

As FeLV is found free in the plasma, as well as budding from leukocytes and platelets in the blood of infected cats, it is conceivable that blood sucking parasites of cats might acquire and transmit FeLV. In warm months flea infestation is very high in the cat population, especially in households with several cats. A hamster reticulum cell sarcoma has been transmitted through the mosquito by transfer of tumour cells[21,22]. We were able to recover FeLV$^+$ leukocytes from a mosquito that sucked blood from an anaesthetized FeLV$^+$ cat with lymphosarcoma. Other cat parasites to be considered as possible vectors are nematodes, coccidia, and rickettsia. It is also quite possible that therapeutic blood transfusions of FeLV$^+$ blood to FeLV$^-$ anaemic cats may account for occasional iatrogenic horizontal transmission of FeLV with the attendant high risk of developing lymphosarcoma. In support of this, we have discovered two FeLV$^+$ normal cats that have repeatedly served as blood donors (see Table 4), but we were unable to identify those cats that received their viraemic blood.

Table 3 Detection of FeLV in Normal Cats from Households with a History of FeLV Associated Diseases

	Number of households in which normal cats were examined	Number of households with FeLV$^+$ normal cats	Households with FeLV$^+$ normal cats (%)	Number of normal cats tested	Number of FeLV$^+$ normal cats	FeLV$^+$ normal cats (%)
Households with a history of feline lymphosarcoma	78	44	56.4	395	154	38.9
Non-cluster households (one case of lymphosarcoma)	50	22	44.0	118	33	19.5
Cluster households (two or more cases of lymphosarcoma)	28 *	22	78.5	277	121	43.6
Households with FeLV-associated diseases other than lymphosarcoma	25	8	32.0	148	23	15.5
FeLV-associated disease households Total	103	52	50.5	543	177	32.6

* Twenty-eight of the thirty-eight lymphosarcoma cluster households (see text) had clinically normal cats.

Table 4 Detection of FeLV in Normal Cats and Frequency of FeLV Infection Correlated with Exposure to Cats with FeLV-Associated Disease

Environment of normal cats	History of FeLV-associated disease in household	Number studied	Number of households with FeLV$^+$ normal cats	Number of normal cats tested	Number of FeLV$^+$ normal cats
Multiple cat households	Yes	103	52	543	177
Multiple cat households	No	47	0	130	0
Single cat households	No	497	0	497	0
Stray cats	—	638	—	638	2 *
Experimental colonies	—	4	0	197 †	0
			Total	2,005	179

* Cats used repeatedly as blood donors.
† Including fifty-four cats from a colony receiving chronic administration of ^{90}Sr.

Implications

Two conclusions emerge from our study. Non-infected cats living in close proximity to cats shedding FeLV have a greatly increased risk of becoming infected and, once infected, the cat has an approximately 900 times greater risk of developing lymphosarcoma.

Whether the exogenous FeLV induces lymphosarcoma, or activates an endogenous virus which does so, is an open question. The important point is that it should be possible to break the cycle of horizontal transmission by vaccination or by selectively segregating or eliminating FeLV$^+$ cats from the cat population. We are now attempting to protect cats at high risk by vaccinating them with attenuated FeLV.

As FeLV replicates so well in human cell tissue culture[23] and as cats live in such close proximity to humans, the question of human infection with FeLV is important. Epidemiological evidence concerning this is inconclusive[24-26]. We have not found any antigen related to FeLV in more than 148 specimens of normal or neoplastic human tissues[7,9] and FeLV antigen has not been found in blood smears from 130 humans, including forty-three individuals living in households with FeLV⁺ cats, fifty-seven veterinary surgeons and thirty employees of veterinary hospitals. Much additional evidence needs to be obtained, however, before concluding that human infection with FeLV-neutralizing antibody exists in human serum. We have recently found that some cats are highly resistant to FeLV and have high titres of neutralizing antibody. A similar response to FeLV infection may occur in humans.

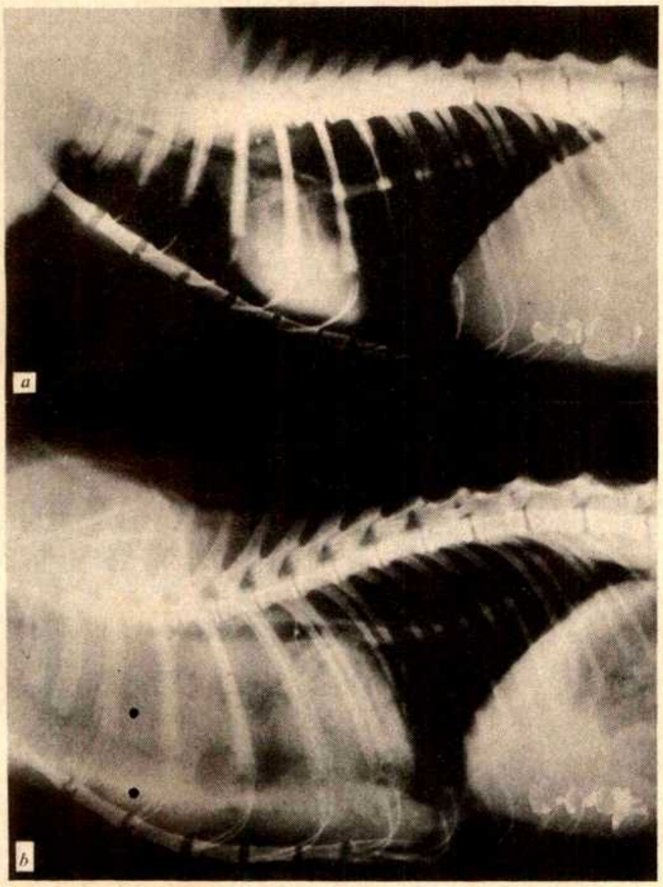

Fig. 2 *a*, Thoracic radiograph of an FeLV⁺ normal cat. There is no evidence of lymphosarcoma. *b*, 3 months later radiographs reveal thoracic effusion and a large anterior mediastinal lymphoid mass.

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Table 5 Summary of Disease Development in FeLV Infected Normal Cats

Result	Number of cats	Cats followed up (%)
Total FeLV positive normal cats	177	—
Follow ups available	148	100
Alive and well	91	61.5
Death due to		
Lymphosarcoma	24*	16.2
Anaemia	11	7.5
Panleukopaenia	13	8.7
Feline infectious peritonitis	5	3.4
Other	4	2.7
Total	57	38.5
Follow-up not available		
Killed while healthy	14	—
Lost contact with owners	14	—
Cat lost	1	—
Total	29	

* The average time required to develop lymphosarcoma after detection of FeLV infection was 5.3 months (range 1 to 24 months).

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LETTERS TO NATURE

PHYSICAL SCIENCES

5 GHz Emission from β Persei

THE triple star system β Persei (Algol) is an erratic radio source[1] which has occasional periods of activity lasting for several days. Jones and Woolf[2] suggest that the emission results from mass transfer between Algol A and B, the components of the 2.8 d eclipsing binary. Hjellming[3] has discussed the parameters of possible models for the emission region.

We report here observations of the source made at 5 GHz during the alignment of the 5-km telescope[4]. These results are of interest not only for the information they provide about Algol itself but because measurements of its position provide a method for determining the coordinate system of the telescope in terms of the position of a fundamental star. The details of the astrometric programme will be reported elsewhere (M. R. and Elsmore, in preparation).

The observations were made between June 1972 and February 1973, and cover about 600 h. On most occasions the flux density was measurable, but it was usually too small for astrometric purposes. Many of the observations lasted for 12 h, but when the nature of the variability became clearer a number of shorter and more frequent observations were made. In this way it was sometimes possible to observe the start of a period of activity and to make more efficient use of the telescope.

The long-term variation in flux density is shown in Fig. 1. Each point represents the mean value during the observing period of up to 12 h, and in addition the maximum range of flux density is also shown whenever significant variations occurred during the observation. The periods of intense activity last for a few days, and are separated by intervals of many days during which the flux density remains at a few per cent of that during the active periods. The present data show no periodic behaviour in the occurrence of these periods.

Figures 2 and 3 show detailed records of observations when the source was active. The flux densities shown in Fig. 2 are running means over 30 min intervals; no significant variations on shorter time-scales are detectable.

The flare of July 11, 1972, is of particular interest because the flux density attained a value (0.65 f.u.) more than twice that observed so far on any other occasion. Figure 3 shows the outburst with both 5 min and 20 min integration. The flux density for 5 h before and 5 h after the flare was less than 0.02 f.u. The flare itself is almost exactly symmetrical, and has a half-intensity width of 50 min. The tail of this flare was observed by Hjellming, Webster and Balick[1] at 2.7 and 8 GHz. We confirm their measured spectral index of $\alpha \approx 0$ (α is defined by $S \propto \nu^{-\alpha}$) near the start of their observations, but as the flare died away the signal to noise ratio became poor and we cannot confirm their report of a significant increase in α at later times.

It seems necessary to suppose that the radiation is generated

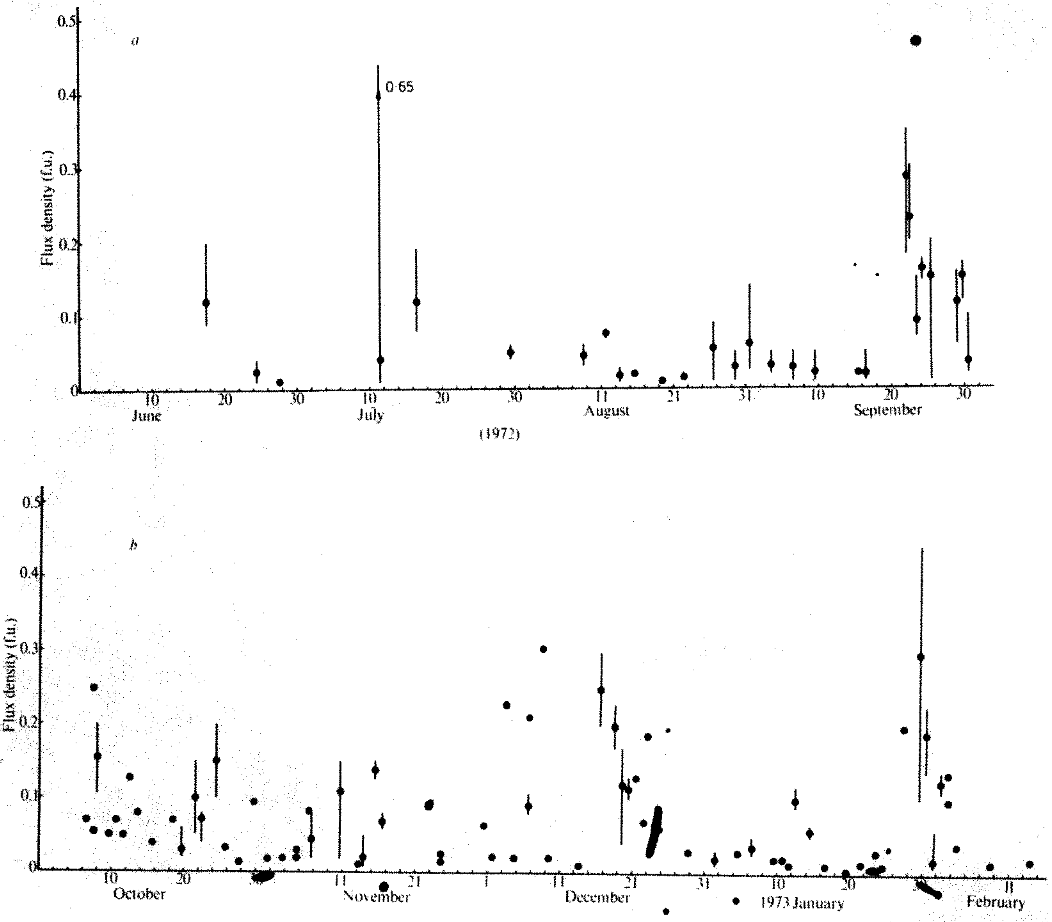

Fig. 1 Flux density of Algol between June 1972 and February 1973. Single values are shown where there was no substantial variation during one observation; otherwise a mean value and overall range are shown.

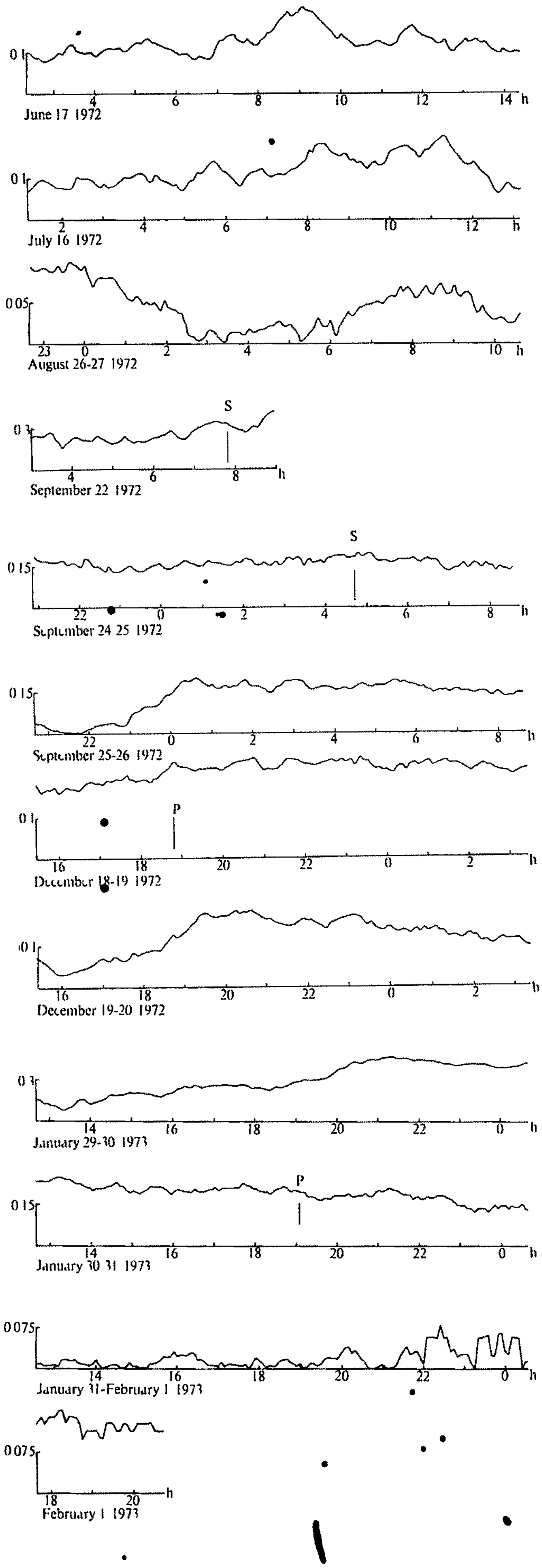

Fig 2 Variation of flux density (f u) of Algol on several days Each record has been integrated for 30 min

in the vicinity of Algol AB, as suggested by Hjellming[3], or the companion Algol C In an attempt to distinguish between these two alternatives, the radio position has been measured, relative to the catalogue position, over a period of seven months Figure 4 shows the means of the measured positions in three intervals of time, compared with the expected orbital positions of Algol AB and C which were computed from the orbital parameters derived by Frieboes-Conde *et al*[5] and Hill *et al.*[6] No account should be taken of the relative zero points of the observed and predicted positions, but the variation of right ascension with time suggests that the emission is indeed associated with Algol AB Further observations over the whole of the 1 9 yr period are needed to confirm this conclusion.

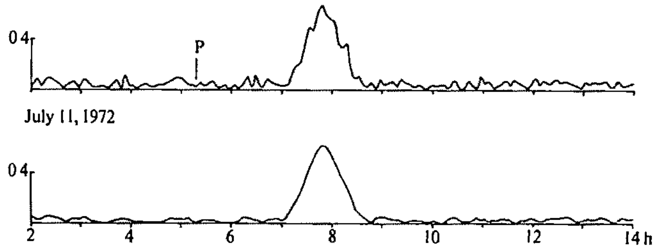

Fig. 3 The event of July 11, 1972, the two versions of the record have integration times 5 min (upper) and 20 min (lower)

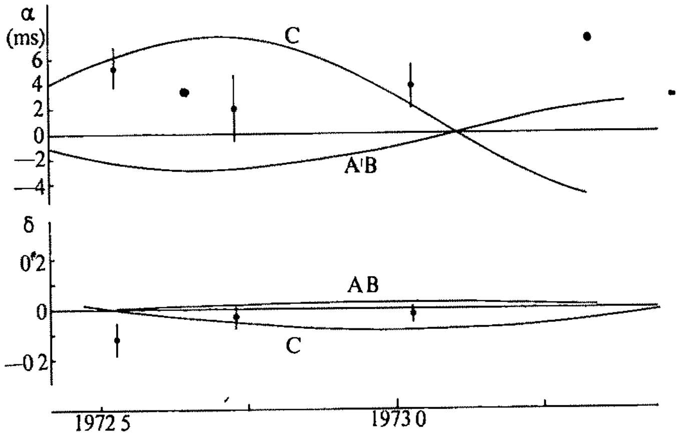

Fig. 4 The position of the radio source relative to the FK4 catalogue position (taking no account of the orbital motion). The curves marked AB and C show the expected orbital positions of Algol AB and C

Information on the size of the source may be obtained from:

(a) Direct measurement of the angular size At no time when the source was intense was there any evidence of resolution by the telescope this sets an upper limit of about 0 7 arc s on the angular size during the active periods. The corresponding limit on the linear size at a distance of 25 pc is 3×10^{12} m, only a little larger than limits set by some of the variations if the excitation is supposed to travel at the speed of light.

(b) Time variations. The most rapid changes occur in about 10 min, implying sizes not more than about 2×10^{11} m for the corresponding emission region, and larger sizes for more slowly varying components As Hjellming, Webster and Balick[1] point out, however, the physical size of an emission region consisting of thermal plasma is likely to be much smaller, because the excitation may only propagate at the speed of sound On such a model the size of the flare of July 11, 1972, would have been about 2×10^{10} m, and on most occasions the source would have been less than about 10^{11} m

(c) Possible occultation phenomena Occultations of the binary system occur every 2 8 d with a secondary occultation almost symmetrically between the primary occultations Because the source of energy is presumably associated with either A or B, it is natural to look for significant occultation effects All occasions on which occultations occurred during an observation have been examined, some are included in Figs 2 and 3, where the times of the primary and secondary occultations are marked P and S There is no substantial decrease in the radio flux density associated with either type of occultation We conclude that the emission region is normally at least 2 or 3 times larger than either Algol A or B (sizes about 2×10^9 m)

The most important restrictions on the size of the source are those set by the time variations ($<10^{10}$ m if heating propagates at the speed of sound, and $<2 \times 10^{11}$ m if heating is by radiation) and by the absence of any significant occultation effects ($\gtrsim 5 \times 10^9$ m) The diameter of the source is therefore fairly closely defined, and is close to the value derived by Hjellming[3] for a thermal source at a temperature of 10^8 K and with $N_e = 10^{10}$ cm^{-3}, presumably occupying part of the space between Algol A and B No clear distinction can be made at present between various mechanisms for exciting the plasma

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Effect of Noble Gases on an Atmospheric Greenhouse (Titan)

MEASURED brightness temperatures of Titan in the 8 to 14 µm range are too high to be produced by simple equilibrium with solar radiation, but at 20 µm the temperature is more in line with the equilibrium value[1,2] An atmospheric "greenhouse" has been invoked to explain these observations, but the amount of hydrogen required to provide the appropriate infrared opacity is much larger than the observed value[3,4] Models including large amounts of helium and methane have been considered by Pollack[5], Hunten[6] has suggested nitrogen as a possible opacity enhancing agent

The true composition of Titan's atmosphere remains obscure Since Kuiper's[7] discovery of methane, only hydrogen has been added to the list of constituents[3] Kuiper's estimate of 200 m amagat for the methane abundance depends on the ambient pressure, which is not known[8], the derived abundance of hydrogen (5 km amagat) has a quoted uncertainty of about 50% and the observation is tentative[3] The presence of other constituents that absorb in the near infrared may be indicated by low resolution observations (ref 9 and R L Younkin, personal communication) Nitrogen and the noble gases would be completely undetectable by present observational techniques

All previous discussions of the atmospheric opacity problem have ignored the possibility[10] that substantial amounts of neon and argon may be present in the satellite's atmosphere If the atmosphere is original, captured from the solar nebula, neon could be more abundant than methane This would result if a large fraction of the original methane were lost as a result of photodissociation and escape of hydrogen with concomitant formation of small amounts of higher hydrocarbons The latter could contribute to the satellite's reddish colour, either as surface deposits or by forming (or colouring) clouds The presently existing hydrogen and methane could then represent an equilibrium mixture which a sufficiently heavy, inert original constituent like neon could now dominate, because its cosmic abundance is only six times less than that of carbon[11] and its atomic weight is sufficiently great to prevent thermal escape[12,13] Neon seems a more likely constituent than molecular nitrogen (which has a comparable cosmic abundance) because nitrogen should be present as ammonia under conditions of chemical thermodynamic equilibrium[14,15] Any original helium would have escaped

The present atmosphere of Titan may be considered alternatively as the result of outgassing by the satellite In that case, some ^{40}Ar would be released into the atmosphere after production by radioactive decay of ^{40}K, as for the Earth Neon will be present in such a secondary atmosphere too as a result of its adsorption on and occlusion in the accreting material that formed the satellite This would also be true for helium, but stability against escape is poor Once again the relative abundances of these gases will depend critically on the subsequent history of the outgassed methane If much methane (factors of ten) has been lost, neon and/or argon could be major constituents in the present atmosphere

With these considerations in mind, we have investigated several models for the atmosphere of Titan that include various combinations of neon and argon Our aim was to see whether the collisional enhancement of the hydrogen opacity would reduce the total amount of hydrogen needed to produce an atmospheric greenhouse effect that was consistent with the infrared temperature measurements Ideally, the model atmosphere would not require the addition of a cloud layer or some other source of opacity to explain the observations

The calculation follows that employed by Cess and Khetan[16] in considering H_2 and H_2–He atmospheres for the major planets We define T_1 as the temperature and P_1 the hydrogen partial pressure at the tropopause, so $T_1{}^4 = T_e{}^4/2(1-2R/C_p)$ and $P_1{}^2 = 8/3\ Ha_1(C_p/R-2)$, where T_e is the effective temperature of the satellite and $H = RT_e/g$ is the scale height The quantity a_1 is determined by fitting an exponential function to the Ne–Ar enhanced hydrogen emissivity which has been evaluated numerically by employing the transition probabilities and rotational line widths of Kiss and Welsh[17] These expressions are valid for Titan providing $a_1 H P_2{}^2 \gg 1$, where P_2 is the hydrogen partial pressure at the surface of the satellite This condition is satisfied for the model atmospheres we consider If we now assume that the lapse rate within the troposphere is adiabatic, then $P_2 = P_1(T_2/T_1)^{C_p/R}$

Table 1 Summary of Greenhouse Calculations for H_2–Ne Atmospheres

Composition Ne/H_2	a_1 km^{-1} atm^{-2}	C_p/R	H km	Surface pressure atm	H_2 abundance km amagat
0	0 68	2 83	249	0 45	340
5	4 6	2.56	29	2 7	40
10	7 9	2 53	27	3 7	28

These relations illustrate that for a given surface temperature, the hydrogen abundance varies roughly as $\sqrt{H/a_1}$ Hence the addition of large amounts of Ne and/or Ar will substantially reduce the hydrogen abundance required for a given greenhouse effect, because H will be reduced while a_1 is increased because of enhancement of the hydrogen opacity Results for H_2–Ne mixtures are illustrated in Table 1 These correspond to $T_e = 90$ K, $g = 150$ cm s^{-2}, and $T_2 = 155$ K, with the latter value selected because of the observed brightness temperatures The same surface temperature has been inferred[5] for H_2–CH_4–He atmospheres Our values of the H_2 abundance and surface pressure for a pure hydrogen atmosphere are in good agreement with Pollack's[5] more detailed calculations Calculated brightness temperatures are compared with observed results for H_2–Ne atmospheres in Table 2

Table 2 Observed and Calculated Brightness Temperatures

Wavelength μm	T_B (observed) K	T_B (calculated) K Ne/H_2 =5	Ne/H_2 =10
8 4	144	143	143
11 0	134	125	126
12 4	125	112	113
20 0	93	97	97

Inclusion of argon reduces the calculated temperatures, which makes H_2–Ne–Ar atmospheres less attractive than the H_2–Ne atmospheres We have not included methane, because Trafton's[8] interpretation of Kuiper's observations[7] implies that methane will be a minor constituent if there is a large amount of neon and/or argon present

The fact that a large amount of neon should be present if the atmosphere is a relic of the solar nebula is an especially attractive feature of these models, because it is hard to justify appropriate abundances of other enhancing agents As in Pollock's models, however, either a cloud or some additional source of opacity is necessary to reconcile observed and calculated H_2 abundances There are indications of clouds on Titan[18-20] and a layer that has a large optical depth in the visible and near infrared but is transparent in the far infrared could "hide" the hydrogen required for the greenhouse while still permitting the reported infrared temperatures to be measured[4,5] With Ne/H_2 = 5, the cloud-top pressure would be 0 34 atm (assuming the observed 5 km amagat of H_2 is all above the clouds) and this is certainly compatible with the observations

Clouds themselves would increase the opacity, thus further diminishing the amount of hydrogen required The composition of such clouds is an open question, methane condensation as proposed by Pollack[5] may not occur when solar absorption by the ν_3 methane band is taken into account The hydrocarbon clouds favoured by Sagan[4] are an attractive possibility, because one certainly expects formation of such substances in this environment Whatever clouds exist must have a very low reflectivity throughout the visible and near IR if they cover a large percentage of the globe[21]

Other gaseous absorbers that might relieve the need for more hydrogen include a number of organic molecules (which might actually be present as aerosols rather than vapours) and H_2S

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Mercury Concentrations in Dated Varved Marine Sediments collected off Southern California

ANNOUNCEMENTS that mercury concentrations often exceed recommended limits in some oceanic fishes, such as swordfish and tuna, have suggested the possibility that man has polluted the ocean with mercury on a massive scale[1] Although there are examples of localized mercury pollution of certain fresh and coastal waters[2-4], there are few data on historical levels of this metal in the marine environment distant from specific inputs such as wastewater outfalls Here we report the concentrations of mercury observed in dated varved sediment layers from the Santa Barbara Basin covering the past 150 yr, as well as in two layers estimated to have been deposited approximately 1,500 yr BP This basin is approximately 100 mile northwest of Los Angeles, and is sufficiently removed from densely populated areas to be protected from the concentrated effects of localized pollutant inputs The record investigated includes layers deposited before the beginning of the California mining activity in 1849 Thus, it has been possible to compare near surface sediment concentrations of mercury with those observed in layers deposited before man could have released significant amounts of mercury directly into the California Current

On most of the ocean floor, organisms living in or near the surface sediment stir the bottom material sufficiently to prevent preservation of any short term record, such as annual variations But in the virtually anoxic Santa Barbara basin off southern California, the lack of active benthic forms has permitted annual variations in the coastal input of sediments to be preserved in an undisturbed sedimentary column Thus, in a manner analogous to the enumeration of tree rings, the varves in such a column may be counted to date a particular layer The correlation of rainfall and sedimentation patterns and ^{210}Pb radiometric ageing[5] confirms these dates

Two different coring techniques were employed to cover different but overlapping time scales A deliberate box corer, designed by A S to obtain sizable cores of soft material without substantial disturbance, was used to obtain samples of recent sediments Three such cores were collected between 1968 and 1971 within 3 mile of each other in the Santa Barbara Basin (approximately 34° 51′ N, 120° 01′ W) at a depth of about 580 m The period covered was 1825 to 1971 A fourth core from the same area, collected in 1966 with a Bootstrap corer[6], obtained a much deeper sample of the sedimentary column The upper portion of this core was identifiable as falling in the period 1820–1845, and thus overlapped the bottom layer in the deepest box core The dating of the bottom layer in this core was less precise, but we estimate it was deposited ~1,500 yr BP

The box cores were frozen on collection, but the Bootstrap core was sectioned and stored unfrozen All cores were subsequently split and X-rayed for detailed examination After correlating unique layers, absolute dates of the varves were established A total of thirty-eight dated subsamples from the four cores were analysed for mercury content Sixteen of these, covering a span of 150 yr, were analysed both by neutron activation analysis (NAA) and by flameless atomic absorption spectrometry (FAAS) The average ratio of the results from these two methods (NAA/FAAS) on the sixteen samples was 1 2, and the 95% confidence interval of the mean ratio was 0 9 to

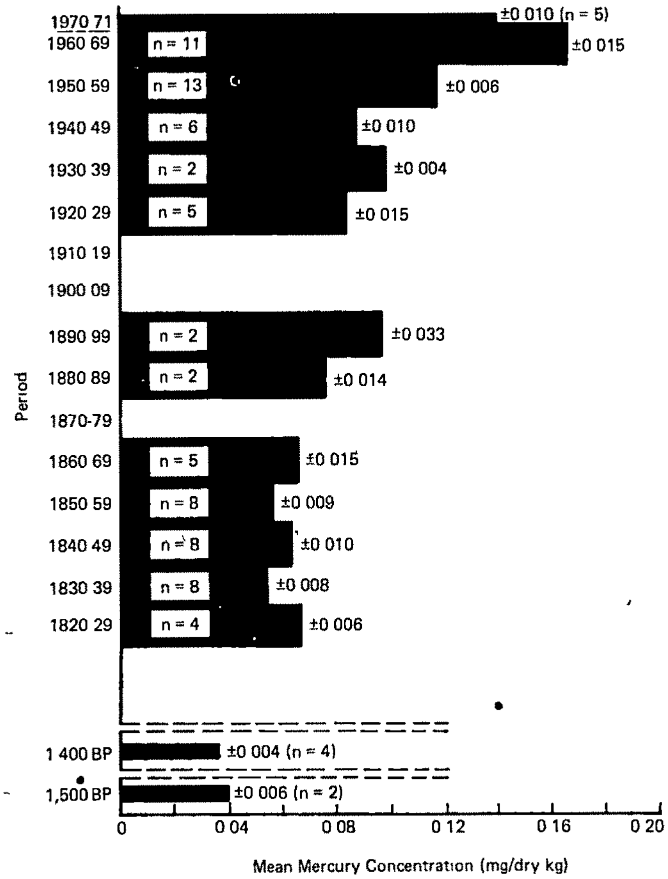

Fig. 1 Mean concentrations of mercury in dated varved sediments from Santa Barbara Basin. Number to right of bar indicates standard error.

1.5. Because the results from the two independent techniques were not significantly different, we consider all the data to be of equal reliability. We note that for each of the decades falling within the periods 1820–1869 and 1920–1971, there are approximately an equal number of analyses by the two methods. The "decade" averages for 1,500 yr BP, 1,400 yr BP, 1880–1889, and 1890–1899, are based on NAA analyses only. In all, concentrations from eighty-five individual analyses were incorporated into the average values for fifteen specified periods. The results (including $s_{\bar{x}}$ and n) are presented in Fig. 1.

The concentrations of mercury in the varved sediments of Santa Barbara Basin show a distinct increase toward the surface. The baseline value for the nineteenth century seems to be $\sim 0.06 \pm 0.01$ mg/(dry kg) with the concentrations beginning to exceed this significantly some time around the turn of the century. In addition, the few samples analysed from the Bootstrap core suggest the possibility of a somewhat lower baseline value for the older sediments. The average value for the layers deposited since 1950 exceeds the estimated nineteenth century baseline value by a factor of approximately two.

This observation may be compared to that of Weiss *et al.*[7] for the concentrations of mercury in dated glacial samples from Greenland. They found a relatively uniform concentration of mercury in layers deposited between 800 BC and 1950, with an approximate doubling in the average value for the past two decades. They attributed this increase to an increased degassing of the Earth's crust, possibly due to the actions of man. Four other investigations into historical concentrations of mercury have also indicated significant increases in recent decades. Thomas[8] reported that the concentration of mercury in a dated core from Lake Ontario began to increase above background levels about 1900, presumably due to the commencement of local industrial discharges. Barnes and Schell[9] observed a similar pattern in three dated cores from Lake Washington. The increases in mercury concentration also began around the turn of the century, and were attributed to a variety of local sources. Aston *et al.*[10] have recently reported that, in a dated core collected from a rural English lake, sediments deposited since 1900 contained approximately twice the average mercury concentration found in sediments laid down during the nineteenth century. They suggested that such mercury profiles in lake sediments are possible indicators of technological growth. Johnels and Westermark[11], working in Sweden, analysed feathers from museum specimens of the great crested grebe (*Podiceps cristatus*), whose diet is principally small fish. Again, the mercury levels began to rise about the turn of the century, and the average value for the past three decades was twice the background concentration. The chlorine–alkali industry, which uses mercury electrodes that permit considerable mercury losses to the environment, was introduced in Sweden about 1900.

Thus, it seems that, during approximately the past 100–150 yr, human activities have resulted in a rather similar pattern of increased mercury introduction to several reservoirs in the northern hemisphere. In those waters relatively close to population centres, increases attributed to various anthropogenic sources are detectable in samples deposited beginning about 1900. In contrast, the levels in the more remote regions of the arctic glaciers reflect a detectable increase only in layers laid down during the past two decades, and this has been attributed to a more general increase in degassing of the Earth's crust rather than specific local or regional inputs. The Santa Barbara Basin dated varved sediments show higher concentrations beginning about the turn of the century, suggesting that increased regional inputs of mercury to the southern California coastal waters occurred about the same time as in several other regions of economic growth in the northern hemisphere. According to this interpretation, the anthropogenic input rate of mercury to this coastal marine reservoir seems roughly to have matched the natural input rate in recent years.

An alternative explanation of the varved sediment mercury profile is that mercury is relatively mobile in the interior of anaerobic sediments and is continuously concentrated in the newly deposited and less anaerobic sediment of the surface layer. At present, the chemistry and mobility of mercury in these marine sediments are too poorly understood to exclude this possibility. Nevertheless, it seems that about a factor of two may be placed on the extent to which man recently has increased, on a regional scale, the level of mercury in the southern California marine ecosystem.

The sediment samples were obtained with the help of Eric Duffrin, and the captain and crew of RV E. B. Scripps. Dr J. Galloway, University of California, San Diego, provided initial guidance in the FAAS measurements. R. Simpson and Deirdre McDermott, Southern California Coastal Water Research Project, provided editorial and technical assistance. This research was supported by the Southern California Coastal Water Research Project and the Marine Life Research Program at Scripps Institution of Oceanography, the latter sponsored by the Marine Research Committee of the State of California.

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Age of the Huntsman Limestone (Bulawayan) Stromatolites

THE Huntsman limestone stromatolites were originally described by Macgregor[1] Recent work (refs 2–5 and T Hoering (personal communication)) has established their organic origin beyond reasonable doubt, and shown that macro, micro and chemofossils occur together in the Huntsman limestone Far less attention has been paid to the stratigraphic and absolute age relations of the limestone in which they occur As a result of recent detailed field work in and around the quarries, and a comprehensive attack on the ages of granitic events in the southern half of Rhodesia, we can now give a revised estimate of the age of these ancient organisms

Cloud[2] crystallized doubts on the true age of the Huntsman fossils when he wrote " the pegmatitic rocks which have been used to place this minimum age (2 6 aeons) on the Bulawayan, occur over 500 kilometres from the stromatolitic structures and there is, therefore, at least a little room for reservation about their age " A further cause for doubt is introduced by the seemingly low grade of metamorphism of the limestone This suggests the possibility that it is a much younger rock, introduced into the area tectonically

The regional geology was mapped and described by Macgregor, Ferguson and Amm[6] The Huntsman limestone was included without question in the lower part of the "Zwankendaba Group" of the Lower Series of the Volcanic Greenstone System, which later became the Bulawayan System (now Group) Lenticular limestone is associated with more persistent Banded Ironstones, and outcrops at intervals for several miles along strike Limestone has been quarried only at Huntsman, and fossils are not known from the other limestone occurrences

Very detailed mapping was undertaken by one of us (N J W) around the Huntsman quarries This has shown that the stromatolitic limestone is interbedded in normal sequence with typical Bulawayan rock types The succession in descending order is

Greenstone
(dolerite sill)
Greenstone
Upper limestone
Banded ironstone
Lower limestone (with stromatolites)
Quartz sericite schist

The field relations are shown in Fig 1

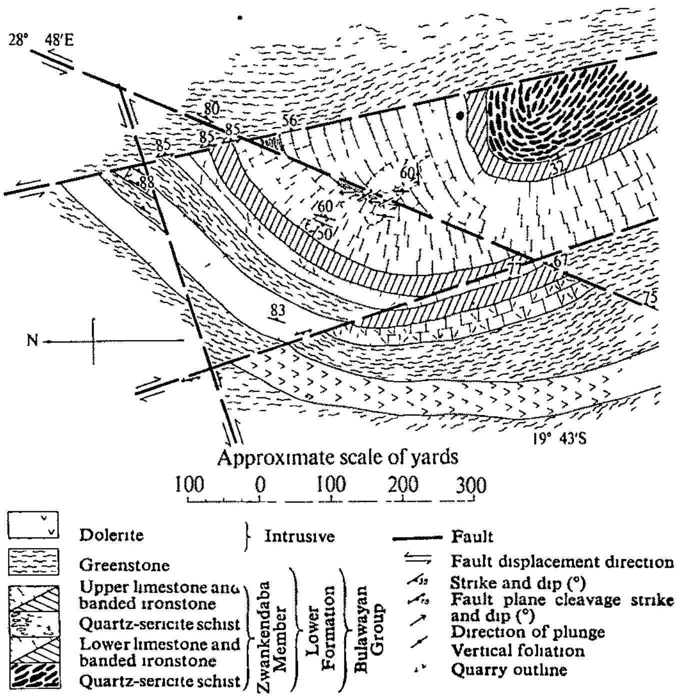

Fig. 1 Field relations, Huntsman quarries

The tectonic style conforms to the general regional pattern of the Bulawayan rocks in the district The area is faulted, but there is no sign of the important structures which would be necessary to implant a slice of much younger rock in the area

The metamorphic grade of the limestone could not be determined directly as no impure carbonate rock with calc-silicate minerals could be found But X-ray diffraction on the insoluble residue shows that some of the carbon is present as graphite, scattered sulphide minerals also occur in the limestone It can be said, therefore, that structurally, stratigraphically and in metamorphic grade the succession which includes the Huntsman limestone is part of the Bulawayan Group in the type area, and lies low down in the succession

The age quoted by Cloud depended upon the age of the Bikita pegmatite 500 km to the east, which is intrusive into what appear to be typical Bulawayan greenstones But lithological correlations of such ancient rocks over such a distance must be treated with caution

Wilson[7] obtained three conventional K-Ar age determinations for each of thirty-nine samples from a variety of granitic rocks in the southern part of Rhodesia Some of these are in the Bulawayo region, and the relevant sample sites, with their ages, are shown in Fig 2 Two other ages which have become known recently are included on the map We list the available information in Table 1

Table 1 Summary of Available Data

Intrusive rock	Age (m y)	
Bulawayo porphyritic granite	2,844 ± 85	K-Ar conventional method
Bulawayo porphyritic granite	2,899 ± 87	
Essexvale granite	2,848 ± 57	
Heany granite	2,962 ± 59	
Hillside syenite	2,603 ± 78	
Formona granite	2,670 ± 110	Rb-Sr

There are, therefore, representatives of both Wilson's $2 9 \times 10^9$ yr and $2 6 \times 10^9$ yr events[7] Because the outcrop of the Bulawayan Group is continuous throughout the area, and the Heany, Essexvale and Bulawayo granites are intrusive into those rocks, we conclude that the age of the Huntsman limestone and its fossils must exceed 2,900 m y, and is probably greater than 3,000 m y This is considerably older than the 2,600 m y minimum age previously assigned to these fossils, and would make them

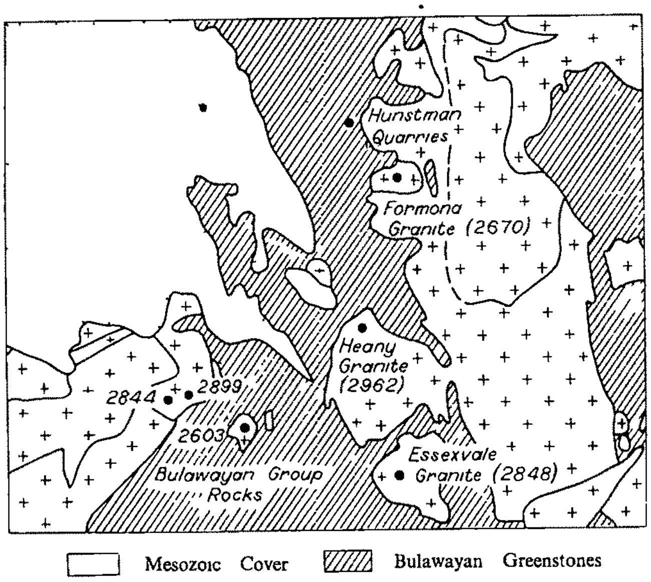

Fig 2 Distribution of dated rocks in the Bulawayo area Scale 1 720,000

the oldest occurrence of combined macro, micro and chemofossils known

It also makes the statement by Molyneux[8] in 1901 that " some of the ancient Rhodesian schists are of sedimentary origin and are worth searching for microfossils " sound almost prophetic

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Syntectonic Recrystallization and Texture Development in Quartz

I HAVE been carrying out an electron microscopy study of quartz which has undergone partial or complete recrystallization during natural deformation This study has shown that syntectonic recrystallization and texture (fabric) development can be interpreted by dislocation processes similar to those observed in deforming metals and ceramics rather than by the crystal growth under non-hydrostatic stress proposed in the literature[1-3]

The quartz specimens used were from the deformed Arunta quartzite, Central Australia[4,5], deformed quartz pegmatites, Ness, Lewis[6], and Moine mylonites, Eriboll, Scotland[7] When examined in a petrological microscope, specimens from the first two localities showed the progressive recrystallization of deformed ribbon-like grains (Fig 1*a*, *b*) which had their *c* axes concentrated perpendicular to their direction of elongation The deformed Arunta quartz grains contained sub-basal deformation lamellae which were gradually replaced by subgrains as the recrystallized areas adjacent to the grain boundaries were approached Only subgrains were observed within the deformed Ness quartz grains and they were of a similar size (20 to 50 µm) to the newly recrystallized grains The outline of relic grains could be distinguished with the aid of a sensitive tint in partially recrystallized areas This suggests that the newly formed grains have orientations similar to their parent grains and become more randomly orientated as the strain increases The mylonite contained small, flattened quartz grains Again a relic structure consisting of larger "streaked out" grains was detected in some specimens, indicating that these mylonites formed by the recrystallization of an earlier structure

Foils representing each stage in the progressive recrystallization seen in the Arunta and Ness specimens, and also from areas in the mylonites exhibiting the relic grain structure, were prepared for electron microscopy by ion thinning All foils were examined in an AEI EM7 electron microscope operating at 1,000 kV The deformation lamellae in the Arunta quartzite were the walls of long irregular subgrains which were subparallel to the basal plane (Fig 1*c*) As the recrystallized areas were approached these shortened first into rectangular (Fig. 1*e*) and then into square (Fig 1*f*) box-like subgrains, by the development of prismatic and rhomb dislocation walls The shortening was accompanied by a progressive rotation of the sub-basal walls into a rhomb position Thus the final product comprised small equidimensional subgrains bounded by walls approximately parallel to rhomb planes These subgrains were much smaller than those seen optically and formed a subgrain in subgrain structure[8] The internal dislocations within the subgrains changed from dense forests of ⟨11$\bar{2}$0⟩ (0001) dislocations (Fig 1*d*) to a low density, recovered structure consisting of bowed, looped and jogged dislocations (Fig 1*f*, *g*) The former dislocation structure caused the undulatory extinction approximately perpendicular to the deformation lamellae Small subgrains with recovered internal dislocations also occurred in the recrystallized grains

The deformed Ness quartz grains had a well developed subgrain in subgrain structure The large more misorientated subgrains (misorientation normally >5°) could be directly related to the optical subgrains The small subgrains within these had only slight misorientations (1° or less) and could not be seen in the optical microscope They contained internal recovered dislocation structures The small recrystallized grains also contained small subgrains with similar internal dislocation structures (Fig 1*h*) In the electron microscope the recrystallized areas could only be distinguished from adjacent parent grains by the preferential etching of their grain boundaries (Fig 1*i*) The mylonite quartz also contained small subgrains with internal recovered dislocation structures

So the recrystallized grains which were seen optically were not strain-free nuclei but clusters of subgrains sufficiently misorientated from their neighbours to be visible as individual entities This clustering was first evident as optical subgrains which apparently became more misorientated and formed the recrystallized grains This type of recovery and recrystallization process obviously differs from static (annealing) recrystallization which produces dislocation-free (strain-free) nuclei[9] It is, however, similar to the dynamic recovery and recrystallization which occur in metals and ceramics during steady state deformation[10-14] and in ice during glacier flow[15] But the textures produced by the two processes differ Static recrystallization results in well defined grain orientations[12] whereas dynamic recrystallization progressively randomizes the texture formed by the intracrystalline slip processes Syntectonic recrystallization is a dynamic process Thus, by combining my observations with the relevant metallurgical data[10-14], a sequence which explains the formation of syntectonic quartz textures can be outlined The stages are the following

(1) Initial deformation by intracrystalline slip This results in a preferred orientation (such as *c* axis maximum texture) of the quartz dependent upon the operative slip system or systems and grain elongation parallel to the local tensile axis Undulatory extinction forms in the grains

(2) Initiation of dynamic recovery This is triggered by the

increase in the internal strain energy of the quartz because of the increased dislocation density. Dislocation movement by cross slip, and particularly by thermally activated processes such as climb, commences. Elongated subgrains form subparallel and perpendicular to major slip planes. There is no change in grain shape or orientation; however, deformation lamellae and deformation bands (narrow elongated subgrains within larger elongated subgrains[8]) form.

(3) Continued recovery and reduction in the internal dislocation density. The elongated subgrains become equiaxed and cluster within higher angle boundaries to form the larger subgrains which can be detected with an optical microscope.

(4) Further recovery. An increasing number of dislocations enter the higher angle boundaries causing the clusters of subgrains to rotate and appear optically as the small recrystallized grains. Because these grains are now individual and distinguishable entities this stage can be termed "dynamic recrystallization". A fine-grained quartz is formed with a crystallographic texture rather similar to that of the former grains, the outline of which can still be detected with a sensitive tint.

(5) Continued rotation and growth of the new grains by stress-induced grain boundary migration. All evidence of the old texture is destroyed. The new texture will become progressively more random as the strain increases; however, the predominance of rhomb and prism boundaries precludes a completely random breakup of the old texture and new textures such as *c* axes, small circles and girdles are formed.

(6) Decreasing rotation and growth of the now enlarged recrystallized grains, The serrated grain boundaries formed by migration interlock and create internal stresses which increase the rate of dislocation generation. These dislocations in turn equilibrate the internal strains in adjacent grains and boundary migration ceases. The increase in intracrystalline slip which may lead to the elongation of the recrystallized grains brings about a further phase of subgrain formation (recovery) and recrystallization—the process recommences.

This sequence is one of continual dynamic recovery of which dynamic recrystallization is a part during a basically steady state flow. There is no sharp demarcation between each stage; one gradually passes into the other. Recovery features can and do coexist with one another, for example, deformation lamellae with subgrains. Individual grains, and even different parts of a single grain, may be at different stages in this sequence due to the inhomogeneity of the local stresses and strains in a deforming polycrystalline body. The predominance of any one of the above six stages during a deformation will depend upon the temperature, strain rate (and differential stress) and, for quartz, the lattice "water" (silanol) content. Low temperatures and normal strain rates or, more particularly, high temperatures and high strain rates will favour stage (1), and quite large grain elongations will be possible before recrystallization. Recovery processes will dominate during the slow deformation of wet quartz at moderate and high temperatures. Exaggerated grain growth can modify the crystallographic texture by eliminating those grains that have rotated into an unfavourable orientation. A high strain rate deformation at moderate to high tempera-

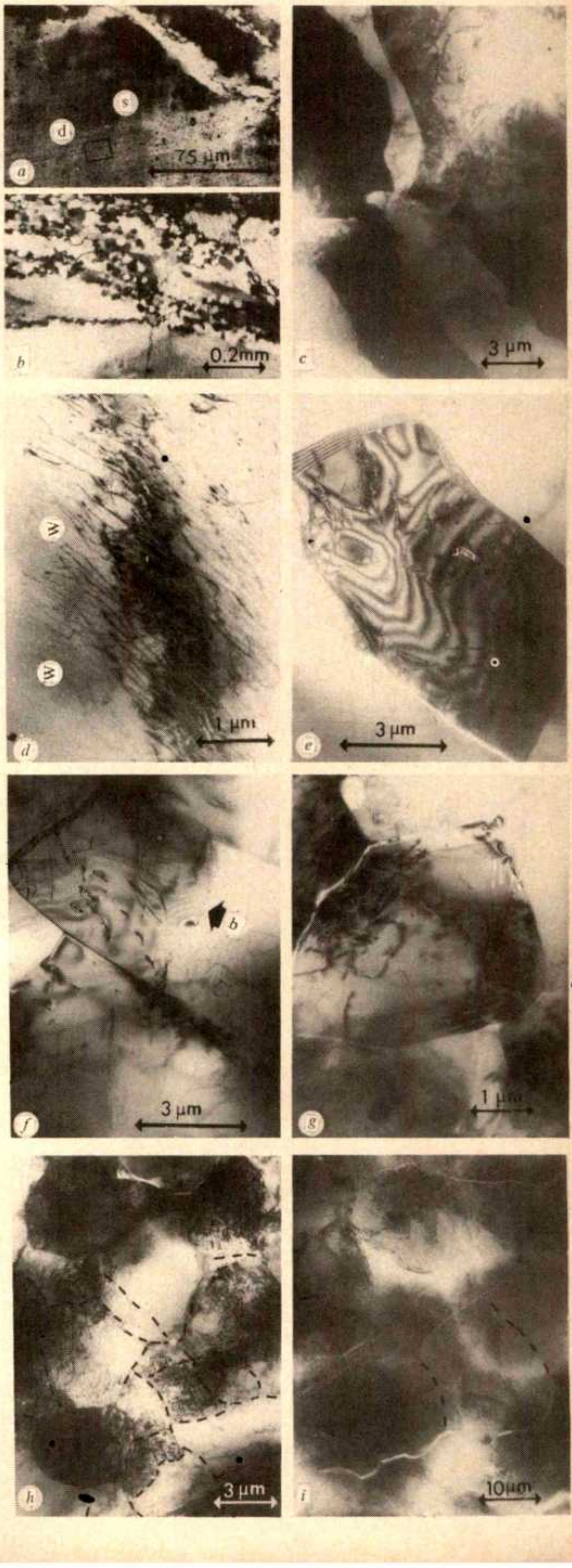

Fig. 1 *a*, Subgrains, s, replacing deformation lamellae, d, adjacent to recrystallized areas in the Arunta quartzite. The marked area in the lower left corner shows the size of the area covered by the micrograph in *c*. *b*, Recrystallized areas in elongated quartz grains in the Ness quartz. *c*, Long subgrains approximately parallel to the basal plane seen optically as deformation lamellae. The dislocations within the central subgrain are out of contrast. *d*, A dislocation forest in a long subgrain. A subgrain wall is visible along ww. *e*, A rectangular subgrain. *f*, The breakup of a rectangular subgrain by an internal low angle boundary, marked b. *g*, An equiaxed subgrain adjacent to a recrystallized area. *h*, Equiaxed subgrains in a recrystallized area. Those subgrain walls that are not clearly visible have been marked in. *i*, Etched out high angle boundaries which surround clusters of subgrains. The marked lines are boundaries which did not etch out completely. (*a* and *b* are optical micrographs; *c* to *i* are electron micrographs; *c* to *g* from the Arunta quartzite and *h* and *i* from the Ness quartz.)

tures should result in cyclic deformation and recrystallization accompanied by progressive grain refinement. Small elongated, rather than equidimensional, grains may form under such conditions. It is possible that many quartz mylonites, especially the primary mylonites along the Moine thrust and in particular the blastomylonites, may have formed by this process, with the grain elongation being parallel to the tensile direction. Larger grains (porphyroclasts) in these mylonites are possible areas at a different phase, or in a different stage in the same phase, of dynamic recovery.

Complications will arise if the temperature or strain rate alters during deformation. If the former drops and/or the latter increases, more dislocations will be generated than can be annihilated by the dynamic recovery processes and the internal dislocation density will increase. A new phase of recovery will be initiated and features such as deformation bands and lamellae or a new phase of recrystallization result. If the operative slip system or systems are temperature dependent then a new crystallographic texture forms in stage (1) and will progressively overprint and eventually replace the existing texture. The overall result is that different textures can arise in separate areas of one rock during a single deformation. Also, deformation features such as lamellae and bands can form at different periods during deformation and cannot be related to any specific strain value.

I suggest that texture development in most crystalline metamorphic quartzites should be interpreted in terms of progressive deformation and dynamic recovery, with dynamic recrystallization being an integral part of the recovery sequence. Also, because the crystallographic texture of a quartz tectonite will depend upon such variables as deformation conditions, operative slip systems, the phase recrystallization preserved, degree of grain growth and the stage at which deformation and metamorphism ceased, as well as the preferential formation of subgrain walls with rhomb and prism walls, it seems unlikely that there should be more than a tenuous relationship between the symmetry of a crystallographic texture and the symmetry of the regional stresses.

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Biological Method of Estimating Smoke and Sulphur Dioxide Pollution

SMOKE and sulphur dioxide levels are measured by the Warren Spring Laboratory at many sites in Great Britain[1], but little information is collected in rural areas. Here we describe a method for estimating atmospheric pollution which can be applied in most areas where trees are found.

Atmospheric pollution has a deleterious effect on much living matter and this may be cumulative[2]. A study of living matter may therefore give an indication of the pollution levels to which an area has been subjected in the recent past. Although effects are seen in animals as well as in plants, the mobility of the former renders them less suitable as local indicators.

Most attention has been paid to the occurrence and growth forms of lichen and bryophyte species (see, for example, refs 3 and 4). Although there seems to be close agreement between these parameters when used as indicators, we are not aware of any attempt to combine several independent measures into a single quantitative assessment. As part of a study of the effects of air pollution on insects[5], we have made measurements at 104 sites in southern Britain of several parameters which may be influenced by air pollution, and here we indicate how they may be combined to provide estimates of smoke and sulphur dioxide levels by multiple regression.

The 104 sites were in closed woodland with a herbaceous understorey. At each, ten oak trees (*Quercus robur*, *Q. petraea* and hybrids) more than 20 cm in diameter at 1 m from the ground were sampled. Homology between the sites was further ensured by the exclusion from the sampling of marginal trees and those bordering pools, streams and marshy areas. The parameters measured in 1969 and 1970 were: the number of bryophyte species present on the boles of the trees; the maximum height at which they were found (excluding rain water runoff channels); the proportion of the bark at 1.5 m covered with algae of the genus *Pleurococcus*, crustose and foliose lichens (the remainder being bare bark); and the mean reflectance of the trunk at the same height. We also included as independent variables the National Grid coordinates of each site (east and north), altitude, mean annual rainfall and mean January and July temperatures[6].

We prepared contour maps for both smoke and sulphur dioxide by extrapolation and interpolation, using the mean annual values published by the Warren Spring Laboratory[1]. To even out the distance between the contours the measure of pollution that we have adopted is the square root of the values (in $\mu g\ m^{-3}$). We see no reason to suppose that the estimates consistently tend to be either too high or too low in either urban or rural areas; the errors will in effect be random and we assume that the only influence on the regressions is to reduce their significance.

With the exception of *Pleurococcus* cover, all the parameters relating to oak trees have high linear correlation coefficients with sulphur dioxide and with smoke (Table 1). The two sets of coefficients are similar because smoke and sulphur dioxide are closely correlated ($r=0.88$). The low values relating to *Pleurococcus* are not unexpected because these algae only occur commonly at intermediate pollution levels.

The multiple regression calculations were performed on a computer using University of California program BMD 02R. The variables which, taken successively, add more than 1% to the value of R^2 (the proportion of the total variance accounted for by the regression) are incorporated into the regression equations in Table 2. In each equation $R^2=0.71$. The constants should be recalculated if the method is used in other situations. Rainfall seems to have little influence on the bryophyte parameters compared with that of pollution; precipitation rates at our sites range from 22 inch yr^{-1} to 90 inch yr^{-1}.

The index y_{SO_2} (Fig. 1) reflects the high levels of sulphur

Table 1 Values of the Correlation Coefficient *r* between the Biological Variables and the Local Pollution Levels at 104 Sites in Southern Britain

	SO_2	Smoke
Species per tree	−0.80	−0.77
Bryophyte height	−0.75	−0.69
Pleurococcus cover	0.12	−0.02
Crustose lichen cover	−0.63	−0.66
Foliose lichen cover	−0.47	−0.39
Bare bark cover	0.72	0.79
Log$_e$ reflectance	−0.76	−0.75

Units of measurement used: smoke and sulphur dioxide $(\mu g\ m^{-3})^{1/2}$; square root of the mean number of bryophyte species on each of ten oak trees; square root of the mean maximum height at which bryophytes were found on each of the ten trees; foliose and and crustose lichens, *Pleurococcus* and bare bark expressed as mean percentile cover at 1.5 m height on the ten trees; mean log$_e$ reflectance of these trees at 1.5 m.

Table 2 Multiple Regression Equations used as an Index of Sulphur Dioxide and Smoke Levels in Figs 1 and 2

(*a*) Sulphur dioxide

$y_{\sqrt{SO_2}} = 17.33 - 1.18 \times \text{spp/tree} - 3.09 \times \text{reflectance} - 2.78 \times \text{foliose}$

(*b*) Smoke

$y_{\sqrt{Sm}} = 9.71 + 4.55 \times \text{bare bark} - 0.82 \times \text{spp/tree} - 2.14 \times \text{reflectance} + 2.33 \times \text{crustose}$

For units of measurement see caption to Table 1.

dioxide occurring in London (Hampstead Heath, J), Birmingham (Edgbaston, E) and the industrial region of Lancashire (Mytholmroyd, A, and Sefton Park, B) and Yorkshire (Tinsley, C). Locally high values, relative to the surroundings, are found in other urban areas, such as Norwich (N), Bristol (Hanham, H) and Bangor (D). A more extensive area where appreciable pollution levels are found is centred on the valleys of South Wales (Pont Rhyd y Fen, F, and Craig Gwent, G). High values of the index found in Ampthill (K), Sandy (L), and Whittlesey (M) are associated with extensive brick making in an otherwise rural area; here fluoride may add to the effects of sulphur dioxide. Because of the absence of National Survey data, we included values not exceeding 30 μg m^{-3} for large rural areas. The index agrees with these lower values for southern England and in Wales. But in East Anglia (such as Upper Sherringham, P, and Woolpit, Q) consistently higher values of y_{SO_2} are obtained.

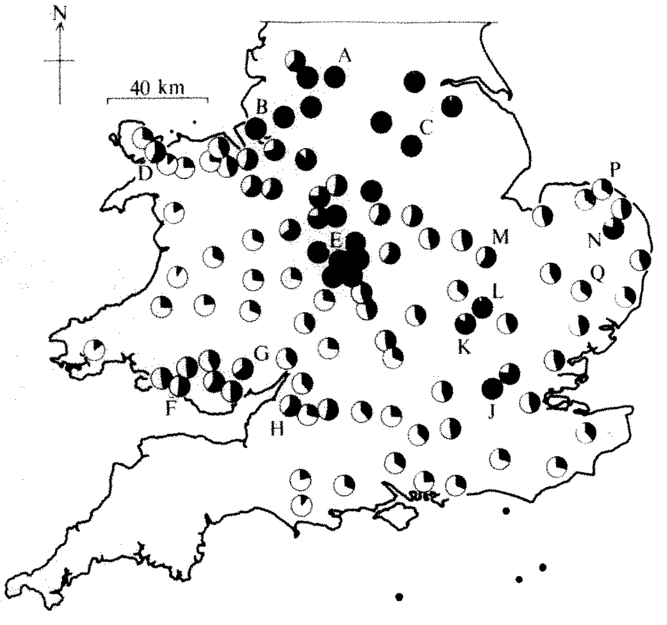

Fig. 1 Map of southern Britain showing values of the index of mean annual sulphur dioxide levels at 104 sites, derived from equation (*a*) in Table 2. The black segments are linearly proportional to the amount of pollutant within the range 0 to 100 μg m^{-3}. Values greater than this maximum are not distinguished. Sites indicated by letters are identified in the text.

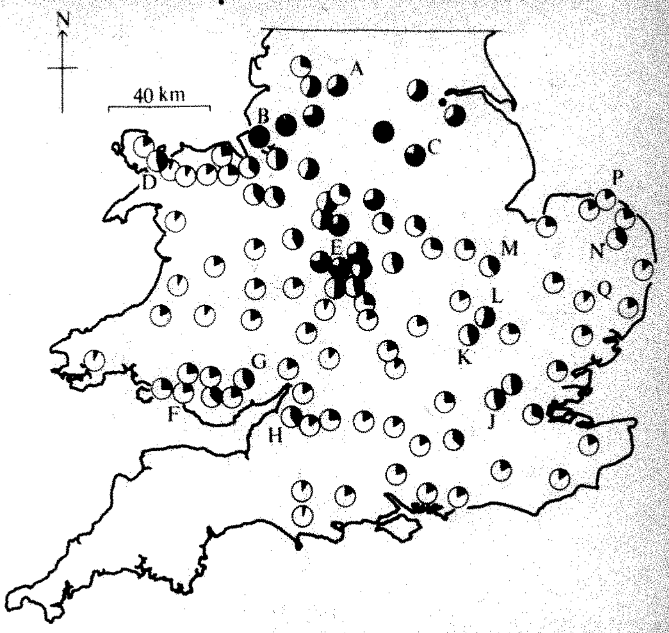

Fig. 2 Map of southern Britain showing values of the index of mean annual smoke levels at 104 sites, derived from equation (*b*) in Table 2. The black segments are linearly proportional to the amount of pollutant within the range 0 to 100 μg m^{-3}. Values greater than this maximum are not distinguished.

Calculated values of y_{Sm} for smoke are shown in Fig. 2. The values reflect the high levels of smoke found in the Lancashire/Yorkshire region (A, B and C) and the progressive decrease in the Birmingham area (E) and in London (J). Locally high y_{Sm} values are also obtained in other areas (D, F, H, K, L, M and N) providing a qualitatively, though not quantitatively, similar situation to that for y_{SO_2}. By contrast with the relatively high values obtained for y_{SO_2} in East Anglia, y_{Sm} is generally low in all extensive rural areas.

The mean number of bryophyte species per tree is closely correlated with the more easily measured mean maximum height at which bryophytes are found on the trees ($r=0.89$); the replacement of number of species by height gives the equations appearing in Table 3 for sulphur dioxide ($R^2=0.69$) and for smoke ($R^2=0.70$).

Table 3 Multiple Regression Equations modified from Those in Table 2 by the Substitution of Mean Maximum Height of the Highest Bryophyte in the Place of Mean Number of Bryophyte Species on Each of Ten Oak Trees

(*a*) Sulphur dioxide

$y_{\sqrt{SO_2}} = 18.72 - 3.94 \times \text{reflectance} - 0.15 \times \text{height} - 2.38 \times \text{foliose}$

(*b*) Smoke

$y_{\sqrt{Sm}} = 9.44 + 5.29 \times \text{bare bark} - 0.09 \times \text{height} - 2.48 \times \text{reflectance} + 2.32 \times \text{crustose}$

For units of measurement see caption to Table 1.

The only survey of Britain comparable with our own is that of Hawksworth and Rose[7]. Although they do not indicate the number of sites surveyed, the detail of their map (Fig. 1) shows a far more intensive coverage than this survey. Quantitative comparison is not possible because they have used mean winter pollution levels whereas we have used mean annual values in calibrating the results. Both surveys show the marked local effects of urban areas. But although Hawksworth and Rose indicate many local effects of air pollution that we have been unable to detect, because of the relatively wide spacing of our sites, their method gives no indication of the apparently high pollutant levels detected by us in the extensive brickfields near Ampthill, Sandy and Whittlesey (K, L and M) and which are in part confirmed by Rose and Pearce[8].

We consider that the method here outlined provides a useful means of assessing long term atmospheric pollution levels. Its advantages over physical methods are that measurements can be made at one time, rather than over a period of at least a year, and separate equipment is not required for each site. By comparison with other biological methods no expert knowledge is necessarily involved in species identification, and a number of independent parameters are combined to provide a single objective estimate. Moreover, detailed local surveys could be undertaken, depending only on the availability of suitable sites.

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Effect of Heat on the Identification of Asbestos by X-ray Diffraction

THE amphibole asbestos minerals amosite and crocidolite have been used for many years as thermal insulating materials, and although their use in new insulation is greatly restricted, they are still found in large quantities in old material. It is necessary to distinguish between the two minerals, because crocidolite has been shown to have a greater health hazard associated with its use[1], and the Asbestos Regulations (1969) require more stringent precautions to be taken when insulation containing crocidolite is being removed. X-ray diffraction is a convenient, and specific, technique for the identification of asbestos in thermal insulating materials. During a recent study of thermal insulation in power stations, many samples were examined which had been at temperatures in excess of 400° C for thousands of hours. The prolonged heating had affected the diffraction patterns.

The action of heat on amphibole asbestos has been investigated in detail[2-4]. At temperatures below 800° C, the chief product is a red-brown oxyamphibole. For amosite, in air, the reaction is:

$$\underset{\text{Amosite}}{\mathrm{Fe}^{2+}_{5\cdot5}\mathrm{Mg}_{1\cdot5}\mathrm{Si}_8\mathrm{O}_{24}\mathrm{H}_2} + \tfrac{1}{2}\mathrm{O}_2 = \underset{\text{Oxyamosite}}{\mathrm{Fe}^{3+}_{2}\mathrm{Fe}^{2+}_{3\cdot5}\mathrm{Mg}_{1\cdot5}\mathrm{Si}_8\mathrm{O}_{24}} + \mathrm{H}_2\mathrm{O}$$

It has been reported[3] that this change results in smaller cell parameters than those of the original amphibole and this is attributed to replacement of Fe^{2+} ions by the smaller Fe^{3} ions.

Standard Asbestos samples of the International Union Against Cancer (UICC) recently became available[5], and the effect of heat on the X-ray pattern of the two amphiboles has been investigated. A series of static ignitions, in air, was carried out at temperatures of 400, 500, 600 and 700° C, the samples remaining at each temperature for 65 h.

Table 1 Change in *d*-Spacings of Amosite with Heat

Peak	*d* spacing (Å) 20° C	400° C	500° C	600° C	700° C
110	8.22	8.22	8.19	8.19	8.18
040	4.540	4.540	4.511	4.466	4.461
240	3.251	3.243	3.232	3.212	3.203
310	3.060	3.060	3.043	3.027	3.023
151	2.755	2.755	2.730	2.710	2.706
061	2.624	2.622	2.605	2.581	2.576
022	2.500	2.500	2.495	2.487	2.487

Table 2 Change in *d*-Spacings of Crocidolite with Heat

Peak	*d* spacing (Å) 20° C	400° C	500° C	600° C	700° C
100	8.35	8.33	8.33	8.33	8.33
040	4.500	4.500	4.473	4.473	4.473
131	3.415	3.395	3.390	3.390	3.390
310	3.102	3.079	3.079	3.079	3.079
151	2.720	2.704	2.704	2.704	2.704
061	2.600	2.588	2.581	2.579	2.578
202	2.531	2.521	2.518	2.518	2.518

The changes observed in the *d* spacings of the principal peaks used for identification are given in Tables 1 and 2.

Care must be exercised when distinguishing between the two forms of asbestos when they may have been subject to heat, particularly when the (310) reflexion is used (this being the reflexion most often used for identification). Some slight changes in the relative intensities of the peaks were also observed. I suggest that several peaks should be used for identification where doubt exists as to the conditions to which the insulation may have been subjected.

It is a matter for some concern that, although a proportion of asbestos-containing thermal insulation has been subjected to prolonged heating at high temperatures, very little has been published about the effect that changes in the structure of the asbestos which occur under these conditions have on its biological properties. Work which has been carried out on chrysotile[6] suggests that further studies in this direction are necessary.

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Reduction of Lens Reflexion by the "Moth Eye" Principle

THE problem of surface reflexion from lenses has led[1] to the development of multilayer interference structures which can suppress the reflexion from glass surfaces by a factor of 10 or more throughout the visible spectrum. But observations on the corneas of nocturnal insects indicate that nature may have anticipated the problems[2]. Electron microscope studies of the corneal lenses of moths reveal that the outer surface is covered in a regular array of conical protuberances, typically of about 200 nm height and spacing. Bernhard[2] proposed that the function of this structure might be to suppress reflexions by effectively proving a graded transition of refractive index between the air and the cornea. The proposal was substantiated by measurements with microwave radiation reflected from a model of the array, scaled up appropriately for the longer wavelengths.

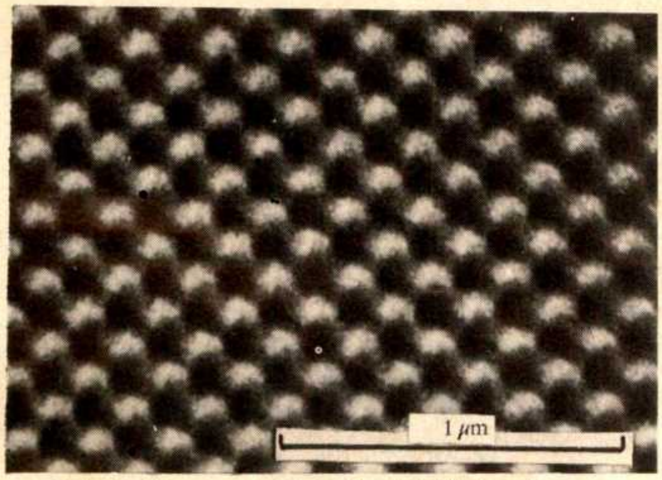

Fig. 1 'Stereoscan' picture of a photofabricated array.

We have prepared a similar array, with dimensions suited to visible wavelengths and have made measurements which confirm the anti-reflexion properties of such a structure. The array was formed in a layer of photoresist coated on a glass substrate, by recording the straight line interference fringes formed at the intersection of two collimated beams of light[3]. In this case the beams were derived from a krypton laser (wavelength 351 nm) and the included angle was about 120°, giving a fringe spacing of approximately 210 nm. The sinusoidal variation of intensity across the fringes was converted, after suitable exposure and development, into a sinusoidal corrugation in the surface of the resist. By superimposing two such patterns at right angles it was possible to produce a surface structure somewhat similar to that described by Bernhard (Fig. 1).

The results of measurements of specular reflectance made at various wavelength are shown in Fig. 2. In making these measurements, the reflexion from the rear surface of the plate was eliminated by blackening, and the reflexion from the photoresist/glass interface was sufficiently small to be neglected. (The glass was chosen to have a refractive index close to that of the developed photoresist, that is about 1.6.) The integrated "white light" reflectance (conditions of photopic visual response and CIE D6500 standard illumination) at normal incidence was reduced from 5.5% to 0.2%. The transmittance of the same plate with the blackening removed showed an increase of 2.5%. This improvement does not match the reduction in reflectance because of absorption losses in the resist. There was no appreciable scattering from the surface although a weak violet diffracted order was visible in the glass. The reflectance from the treated surface can, in principle, fall to zero for all visible wavelengths if the geometry of the structure is optimized. The dependence of the reflectance on the effective thickness (*d*) of the layer of graded refractive index and on the wavelength (λ) of the light was investigated by Rayleigh[4], and we have computed similar results by representing the graded interface by many layers of equal thickness and progressively increasing refractive index (Fig. 3). When $d \ll \lambda$ the interface appears relatively sharp, and the reflectance is essentially that of a discontinuous boundary. As d/λ increases, however, the reflectance falls monotonically to a minimum value at $d/\lambda \approx 0.4$. Further increases in d/λ show a series of successive maxima and minima in reflectance, but nowhere does the value approach that of the sharp interface. When $d \ll \lambda$, the reflectance is essentially zero. Thus for optimum performance in the visible region of the spectrum, the thickness of the gradient (the height of the protuberances) should be 250 nm or more. In our case, the significant reflectance and its increasing value for longer wavelengths suggests a thickness rather less than this was obtained. The spacing of the protuberances must clearly be sufficiently fine to avoid losses by diffraction, that is, it must be less than the shortest wavelength involved divided by the refractive index of the material, in practice about 250 nm.

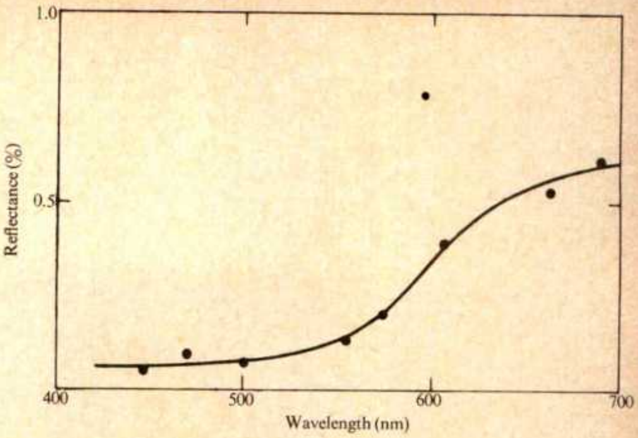

Fig. 2 Measured specular reflectance (normal incidence).

In its optical performance the dimpled surface offers an attractive alternative to multilayer antireflexion coatings. The suppression of reflexion over a wide spectral range is comparable with the best multilayer coatings commercially available. Although we have demonstrated that it is possible to produce such a surface, our experiments have been restricted to plane surfaces, and the resulting "coatings" have been extremely delicate. Clearly, considerable techno-

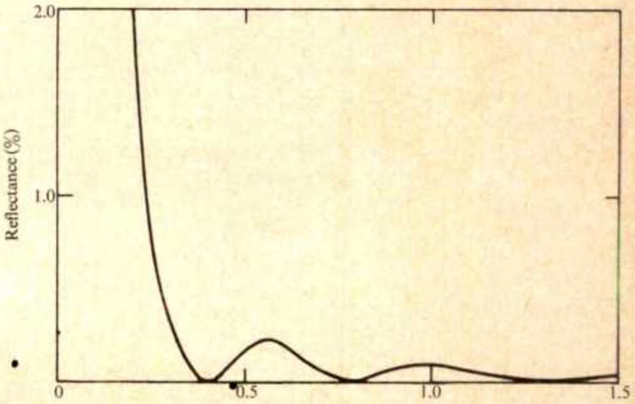

Fig. 3 Computed dependence of reflectance on d/λ.

logical development would be required before the process could become a practicable alternative to multilayer coating.

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Ion Microprobe Confirmation of Pb Isotope Ratios and Search for Isomer Precursors in Polonium Radiohaloes

RADIOHALOES associated with decay of several Po α emitters[1,2] have been studied by optical microscopic techniques and more recently by mass spectrometric examination of the halo inclusion using ion microprobe techniques[3,4]. In such cases a large excess of ^{206}Pb compared with ^{207}Pb was found to be incompatible with the radiogenic decay of ^{238}U and ^{235}U, yet was explainable on the basis of polonium decay independent of uranium[3]. A straightforward attempt to account for the origin of these Po haloes by assuming that Po was incorporated into the halo inclusion at the time of host mineral crystallization meets with severe geological problems: the half-lives of the polonium isotopes ($t_{\frac{1}{2}} = 3$ min for ^{218}Po) are too short to permit anything but a rapid mineral crystallization, contrary to accepted theories of magmatic cooling rates.

This dilemma might be resolved (R. V. G., unpublished) if several long half-life high-spin or shape isomers of polonium (or the β-decaying precursors) were formed at nucleosynthesis and were subsequently incorporated into the halo inclusions during crystallization. This hypothesis eliminates the geological difficulties, and is open to experimental verification using several techniques such as charged particle reactions, though the long half-lives may present an obstacle. But long half-lives imply that some of the isomers may still exist, in which case a mass analysis of the polonium halo inclusions should reveal whether significant quantities are still present. We now report additional ion microprobe analyses of these Po inclusions as well as U inclusions in search of the isomers and for additional information on the Pb isotope ratios.

Mass scans were taken on areas of the biotite free from haloes All the normal elemental constituents as well as some trace elements were seen in these scans. The mass region from 150 to 300 is conspicuously free from any mass peaks. Generally Fe_2^+ at position 112 is the only high mass peak of significance observed from the biotite itself.

In the pure uranium, thorium, or uranium-thorium inclusions, ion microprobe analysis showed that the inclusions were either zircons or monazites; in many cases the ^{204}Pb ion current or signal was near background, so that it was difficult to make a common Pb correction; the ^{238}U/^{235}U ratio was normal in inclusions which contained uranium; and the ^{238}U/^{206}Pb signal ratio varied from 10 to 70 in the different inclusions analysed. The actual ^{238}U/^{206}Pb atom ratio is difficult to determine because of the uncertainty in the U and Pb secondary ion yield from different minerals. In general, U is detected with several times greater efficiency than Pb. The radiogenic ^{206}Pb/^{207}Pb ratio was difficult to evaluate in those inclusions where the ^{204}Pb signal was near background. In other cases it was found to vary within normal limits.

There is a wide spectrum in the U and Th halo types—some inclusions contain just U or Th without the other element, while other inclusions contain varying amounts of U and Th and in some cases exhibit rings from both decay series; it seems that the same situation prevails with Po and U type haloes in certain micas. In the analyses thus far it seems that the larger the Po halo inclusion the greater the U content tends to be; but more work is needed to verify this. Also the larger inclusions seem to be definite mineral types (usually rare earths but not specifically identified as yet), whereas some of the point-like Po halo inclusions consist of only elemental Pb (without ^{204}Pb) and Bi. Previously no detectable U was found in such cases as the latter type.

In contrast to the Pb ratios in the U and Th halo inclusions, we again report exceptionally high ^{206}Pb/^{207}Pb ratios which are characteristic of the ^{218}Po decay sequence type Po halo. The results may be summarized as follows: ^{206}Pb/^{207}Pb ratios of 10, 12, 18, 22, 25, 40, and 100 were observed. In four of these cases no ^{204}Pb was detected. In the other two cases ^{204}Pb was almost background, so that no common Pb correction was made on any of the ratios (any such correction would have produced a larger ^{206}Pb/^{207}Pb ratio). In three of the cases (10, 12, and 22) the small uranium signal seen was 10 to 100 *times less than that* required to support the Pb observed. These results confirm the earlier ion microprobe analyses of Po halo inclusions in which Pb ratios were found that were impossible to explain on the basis of U decay. They give confidence that we are indeed dealing with a class of haloes that is distinct from the ordinary U and Th types as the optical microscopic measurements invariably suggest. Otherwise, the most important aspect of the results is that the decay product of the polonium (Pb) still exists in these inclusions in measurable quantities (10^8–10^{10} atoms) and has not diffused away. On such a basis we then expect that any isomer precursor of Po, if the half-lives were sufficiently long, would also still exist and be detectable by ion microprobe techniques.

The only source of geochemical data about the postulated isomer is derived by inference from the type of halo inclusion. Some Po halo inclusions are of the rare earth variety while others contain only elemental Pb and Bi. The latter case might suggest the existence of an isomer geochemically similar to those elements, whereas the former case is rather non-specific. Fortunately ion probe mass analysis techniques do not depend on knowing the chemical identity of the postulated isomer.

To obtain these Pb ratios, we first cleaved the mica until the halo inclusion appeared on the surface. In some cases the sample was coated with a thin conducting layer of carbon, but it was better to overlay the sample with electron microscope-type Cu grids. In the latter case there was no extraneous material introduced anywhere near the region of interest. Before taking mass scans on the Po haloes the ion microprobe was optimized to obtain the best Pb signal from large U type halo inclusions that were mounted on the same sample but in a different area. In many cases the ion probe was peaked on mass 206 position and then moved to the area in the vicinity of the Po halo inclusion. The signal at this mass position remained at background (1 Hz) until the beam was shifted to the Po inclusion itself. In some cases several minutes elapsed before the signal reached maximum intensity. Generally mass positions 204, 207, 208, 218 and 238 were monitored, as well as the regions considerably below Pb, for possible interference from molecular ions. In other cases mass scans of the entire region from mass 1 to 250 were taken. It can be definitely stated that the exceptionally high 206 signal, compared with 207, occurs only in the Po halo inclusions and is not an artefact due to a molecular ion originating with the mica itself, the inclusion, or a combination of the mica and the elemental constituents of the inclusion. This is not to say the ion microprobe does not generate molecular ions, for in certain cases it does so very efficiently. But in the case of the Po haloes, we took care to monitor the various possibilities, which could have interfered with the results

The search for the isomer consisted of carefully scanning the region around mass 218, for the Po haloes used in these experiments originated with ^{218}Po α decay To be certain of the mass position, a small amount of Hg was placed on the sample holder to use as a mass marker at the 218 position (^{202}Hg^{16}O) In all Po inclusions except one no signal was observed at the 218 position That one exception was due to interfering HgO ions from the presence of Hg in the inclusion itself

A very rough estimate of what these results mean in terms of the present existence of the isomer in the inclusion may be obtained because the ^{206}Pb sputtered ion count rate was greater than 1,000 Hz in some Po inclusions If it is assumed the isomer resembles Pb in sputtered ion efficiency (Pb has a relatively poor sputtered ion yield), then the present abundance of the isomer in the inclusion is $\leqslant 10^{-3}$ that of the ^{206}Pb One interpretation of these results is the isomer has simply decayed to the point where it was not detected in these experiments (These samples were from an early Precambrian pegmatite in Scandinavia) It is yet to be determined whether this information is consistent with the half-lives of the proposed isomers that can be ascertained by determining the latest geological epoch in which such haloes occur

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BIOLOGICAL SCIENCES

Hypermethylated tRNA in Cleaving Rabbit Embryos

THERE is evidence of a significant transition in the growth characteristics of the mammalian embryo shortly after the onset of blastocyst formation[1-3] In those mammals displaying "delayed implantation", extended periods of reversible growth arrest can occur at this time[4] In the rat, this arrest is clearly a function of embryonic development cleavage is uninhibited by the hormonally deprived uterus, and arrest occurs only with blastocyst formation[5] The rabbit embryo, which does not display reversible arrest, nonetheless develops to the early blastocyst stage under various abnormal conditions[6,7], whereas further progress to implantation requires, at least transiently, a more complex environment[8] The molecular basis of this transition in embryonic behaviour in mammals is, therefore, relevant to the problem of the control of cell division Developmental transitions in a number of biological systems have been found to be accompanied by alterations in the tRNA methyltransferases and in populations of tRNA[9], and as tRNA synthesis begins shortly after fertilization in mammalian embryos[10,11], we have examined the methylation of tRNA during the preimplantation development of rabbit embryos as an approach to understanding the transition in embryonic growth characteristics Our findings provide evidence for a marked decrease in tRNA methylation with blastocyst formation

Preimplantation embryos were exposed to radioisotopes in F-10 solution[12] modified by the inclusion of 10^{-2} M HEPES buffer (Calbiochem) and 5 mg ml^{-1} dialysed, lyophilized rabbit serum Embryonic age was estimated by assuming egg fertilization to have occurred 12 h *post coitum*[13] During labelling, embryos were maintained at 38° C in an atmosphere of 5% carbon dioxide in air at saturation humidity After extensive washing in saline and homogenization with rabbit liver as carrier, the homogenate was centrifuged at 20,000*g* for 15 min, and RNA was extracted from the supernatant by the method of Oda and Joklik[14] as modified by Kabat[15] Electrophoretic separation of RNA on 2 5% polyacrylamide gels was carried out as previously described[10] Precursor uptake into the acid-soluble pool was determined by rapidly washing labelled embryos, freezing and thawing them six times in distilled water, and measuring radioactivity in an aliquot of the supernatant following overnight precipitation in 0 3 N perchloric acid and centrifugation at 20,000g for 20 min Larger blastocysts were removed from the zona pellucida and washed free of blastocoelic fluid before freezing

The simultaneous labelling of embryonic tRNA with ^{32}P-phosphoric acid and L-methionine (^{3}H-methyl) facilitates a comparison between the rate of synthesis of the nucleic acid polymer and the rate and extent of its subsequent methylation in the intact embryo ^{32}P-labelling of tRNA represents true synthesis at all early stages of rabbit embryogenesis, rather than turnover at the –CCA terminus It is inhibited by actinomycin D[10] and is resistant to *Crotalus* venom phosphodiesterase. The kinetics of uptake of L-methionine and phosphoric acid were similar in cleaving embryos and early blastocysts, pools were saturated by the second hour Possible variations in precursor pool size at different stages of embryonic development were taken into account by determining the ^{3}H/^{32}P ratio in the acid-soluble fraction The ^{3}H/^{32}P ratio in the counts recovered from the 4S region of polyacrylamide gels, corrected by the ^{3}H/^{32}P ratio in the acid-soluble fraction, indicates the extent of methylation of newly-synthesized embryonic tRNA The tRNA methylation decreases approximately six-fold between the fifty-second and eighty-fourth hours of embryonic development (Table 1), a period which coincides with blastocyst formation

As blastocysts display greater amino acid uptake and incorporation *in vitro* than cleaving embryos[1], the decreased methylation of tRNA in blastocysts is not due to a loss of viability under culture conditions The ^{3}H radioactivity in tRNA represents methylation rather than labelling of the purine or pyrimidine rings 5S RNA, which is not known to be methylated in other cells, had no ^{3}H radioactivity in these experiments

Embryonic tRNA labelled with L-methionine (^{3}H-methyl) alone was analysed for various methylated constituents (Table 2) In 72-h embryonic tRNA, 1- and 7-methylguanine comprised about 1% of the total methylated bases After 12 h of development, a twelve-fold increase in the proportion of these constituents was found Alterations in other methylated bases were also observed The earliest embryonic stage from which sufficient ^{3}H radioactivity could be recovered for base analysis was the early blastocyst at 72 h following fertilization It would be of interest to examine the methylated bases at earlier stages The low levels of total incorporated radioactivity in cleaving embryos, however, would necessitate using very large numbers of animals to acquire that information

The rate of tRNA synthesis and its methylation, as well as the analyses of methylated constituents in the tRNA, relate to

Table 1 *In vivo* Labelling of tRNA during Pre-implantation Rabbit Development

	Embryonic age (h following egg fertilization)				
	52 (late cleavage)	60	84 (early blastocyst)	108 (late blastocyst)	132
Embryonic cell No (approximate)	64	128	1,024	9,000	80,000
Total No of embryos used	63	51	59	36	18
^{3}H/^{32}P c p m incorporated into tRNA / ^{3}H/^{32}P c p m in acid-soluble fraction	22 5	14 5	3 7	3 6	2 2

Embryos were exposed to carrier-free ^{32}P-phosphoric acid (500 µCi ml^{-1}, New England Nuclear Corp) and L-methionine (^{3}H-methyl) (200 µCi ml^{-1}, 3 3 Ci mmol^{-1}, Schwarz/Mann) simultaneously in phosphate-free and methionine-free F-10 solution[12] for 4 h RNA was extracted as described and separated electrophoretically on 2 5% polyacrylamide gels 4S RNA was excised from these gels and ^{3}H/^{32}P radioactivity determined by the method of Tishler and Epstein[21] The ^{3}H/^{32}P ratio in the acid-soluble fraction was determined at the mid-point of the labelling period, when precursor pools were found to be saturated The kinetics of uptake of methionine-^{3}H and ^{32}P were similar in cleaving embryos and early blastocysts Each value is the average of two determinations

Table 2 Analysis of Methylated Constituents in tRNA of the Pre-implantation Rabbit Embryo

	Embryonic age (h following egg fertilization)			
	72	84	108	132
	(early blastocyst)		(late blastocyst)	
Total No of embryos used	130	62	60	28
^{3}H c p m in tRNA	4,500	7,000	9,500	12,300
Methylated constituents				
Methylated cytidylic acids	24	26 7	25 2	10
Methylated uridylic acids	14 5	29 7	15 6	16 2
1- and 7-methylguanine	1	12 4	19 9	13 1
N^2-methylguanine	21	15	15 3	26 3
N^2-dimethylguanine	16	5 4	9 3	11 5
1-Methyladenine	22 1	9 3	12	21 2
6-Methyladenine	0	1 4	2 8	1 5

Embryos were exposed to L-methionine (methyl-^{3}H) (400 µCi ml^{-1}, Schwarz/Mann) in methionine-free F-10 solution[12] for 6 h Cytoplasmic RNA was extracted as described, purified on a DEAE cellulose column, treated with pancreatic DNase (RNase-free, Worthington) and pronase (Calbiochem), deacylated and isolated by gel filtration on 'Sephadex' G100 Acid hydrolysis and thin-layer separation of methylated constituents were carried out by the method of Bjork and Svensson[22] The values have been expressed as percentage of radioactivity recovered, and are the average of two determinations 1-Methylguanine and 7-methylguanine were not adequately separated in most of the analyses, and these values are given collectively

total tRNA isolated from the entire embryo Differences in methylation patterns between differentiating embryoblast and trophoblast cells would not be detected, nor would subtle differences in the methylation of individual tRNA species During preliminary experiments, we found that the relative proportions of individual methylated bases fluctuated in response to differing conditions of *in vitro* labelling The data reported here, using standardized *in vitro* conditions which are compatible with extended periods of embryonic survival, reflect changes in embryonic tRNA methylation primarily as a function of embryonic age tRNA synthesis[16] and alterations in tRNA methylation have also been observed very early during sea urchin embryogenesis[17]

The hypermethylation of tRNA in the cleaving rabbit embryo resembles that demonstrated in "transformed" and neoplastic cells[9] The transition in embryonic growth characteristics with blastocyst formation is accompanied by a marked decrease in tRNA methylation Methylated bases of tRNA are known to be determinants in amino acid acceptance[18], codon response[19] and ribosomal binding[20] Thus, decreased methylation in rabbit embryos may be directly and causally related to the acquisition of heightened responsiveness to regulatory influences in the reproductive tract

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Increase in Histamine Receptors on Thymus-derived Effector Lymphocytes during the Primary Immune Response to Alloantigens

THE cytolysis of alloantigen-bearing target cells by thymus-derived (T) lymphocytes from appropriately immunized animals has particular relevance to allograft rejection (see ref 1 for review) Although the mechanism of lysis remains imperfectly understood, recent studies suggest that it consists of multiple steps[2–4] triggered by antigen-lymphocyte interaction[5], which terminate in the secretion of a cytotoxic mediator protein into or onto the membrane of the target cell[6,7]

Drugs which stimulate lymphocyte adenylate cyclase, and thereby increase the intracellular level of cyclic 3′,5′-adenosine monophosphate (cyclic AMP), inhibit cytolysis[8–10] This process is reversible, inhibition of cytolysis lasts only as long as lymphocyte cyclic AMP levels are elevated Among the drugs shown to raise lymphocyte cyclic AMP and inhibit T cell-mediated cytolysis are prostaglandins E$_1$ and E$_2$[9], cholera enterotoxin[10,11] and histamine[9] PGE$_1$ and cholera enterotoxin can totally inhibit cytolysis, while histamine and the catecholamines are only partially suppressive[9]

Histamine stimulates adenylate cyclase through a specific receptor, presumably located on the cell membrane, as has been directly demonstrated[12–14] On pharmacological evidence, Ash and Schild[15] postulated that there are two or more different classes of histamine receptors on cell surfaces, and supporting data have been provided by Black *et al* [16] using the histamine antagonist burimamide Antihistamines such as diphenhydramine block what are designated histamine 1 receptor sites, which are responsible for mediating bronchial and ileal smooth muscle contraction, while burimamide blocks the action of histamine in increasing gastric acid secretion and relaxation of the rat uterus, but has little or no effect on histamine 1 activities[16,17] Sites antagonized by burimamide have been designated histamine 2 receptor sites

We have demonstrated that the ability of histamine both to inhibit lymphocyte-mediated cytolysis and to augment cyclic AMP levels in murine spleen cell suspensions could be specifically antagonized by burimamide, but not by antagonists of histamine 1 receptors, for example, diphenhydramine[18] This has provided evidence for the concept of histamine receptor units on the membranes of cytolytically active lymphocytes, and has established that these receptors are of the histamine 2 type As noted, our previous observations have shown only a partial inhibition of cytolysis by histamine, moreover, the degree of inhibition noted was more variable from experiment to experiment than that seen with other agents This suggested to us that there was a relative paucity of histamine receptor sites on cytolytically active cells and that the number of these sites might vary as a function of cellular differentiation The study reported here was undertaken to follow the appearance of histamine receptor structures on effector T lymphocytes We found that the susceptibility of cytolytically active cells to suppression by histamine *in vitro* increased markedly with time following primary alloantigenic stimulation We suggest that this altered susceptibility is due to an increase in the proportion of effector cells bearing histamine receptors

C57Bl/6 mice were immunized intraperitoneally with 10^7 DBA/2 mastocytoma cells (P815)[19,20] At various times following this immunization, groups of immune mice were killed, and single cell preparations made from their spleens[20] Mastocytoma cells (carried in ascitic fluid of DBA/2 mice) were collected and labelled with ^{51}Cr-sodium chromate ('Rachromate', Abbott Laboratories, Chicago)[19] Cytolytic activity was assayed by mixing 10^7 splenic lymphocytes with 10^5 ^{51}Cr mastocytoma cells in 1 ml Eagle's minimal essential medium containing 10% inactivated foetal calf serum and 100 IU ml^{-1} both of streptomycin and penicillin[19,20] Incubation was carried out for 4 h at 37° C in an atmosphere of 5% CO_2–95% air Following incubation, the cells were centrifuged and an aliquot of the supernatant assayed for ^{51}Cr content The percentage specific lysis was obtained after subtracting the percentage lysis in control tubes containing normal (non-immune) lymphocytes[20] The effect of histamine on cytolysis was measured by mixing together the lymphocytes, mastocytoma cells, and appropriate concentrations of histamine HCl (Sigma) at the start of incubation The effect of burimamide (given by Dr J W Black, Smith, Kline and French Laboratories, Hertfordshire) on cytolysis was studied similarly, by addition of appropriate concentrations of burimamide with or without histamine, at the start of incubation The percentage inhibition of cytolysis in each case was calculated relative to lysis in the absence of drugs[9]

Cyclic AMP assays were performed by incubating 10^7 splenic lymphocytes, with or without histamine, in 1 ml Eagle's medium containing 10% inactivated foetal calf serum for 10 min at 37° C The cell suspensions were then centrifuged and the cell pellets resuspended in 0 5 ml 5% trichloroacetic acid The cyclic AMP content of the resulting suspension was determined by the method of Brown *et al*[21]

The inhibition by histamine of the cytolytic activity of lymphocytes obtained from mice immunized 9–17 d previously is shown in Fig 1 The linear regression line demonstrates that there is a highly significant, positive correlation (r=0 82, P<0 001) between the time following immunization, and the susceptibility of cytolytically active cells to suppression by histamine The altered susceptibility to histamine was associated with only a modest change in cytolytic activity For example, 10 d after antigen administration, the percentage specific cytolysis was 37±3% (s e m), such cytolysis was inhibited only 11±2% by 10^{-5} M histamine Fourteen days after immunization, the percentage specific cytolysis was 26±3%, while inhibition of cytolysis by 10^{-5} M histamine had increased to 35±4% This phenomenon is further illustrated by the experiments represented as solid circles in Fig 1 In these studies, animals were immunized simultaneously and then sequentially killed Inhibition of cytolysis by histamine increased throughout the period of study (10–17 d), and was demonstrable with concentrations of histamine ranging from 10^{-7} to 10^{-3} M (see also Table 1)

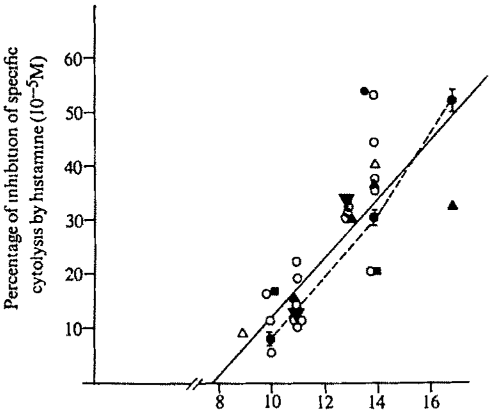

Fig. 1 Adult C57Bl/6 mice were immunized intraperitoneally with 10^7 DBA/2 mastocytoma cells The cytolytic activity of spleen cell suspensions was assessed at various times thereafter (see text), and the inhibition of cytolysis by 10^{-5} M histamine measured on each occasion Data from thirty experiments are shown together with the linear regression line for all the data ○, Animals were tested on day one only, in these cases, lymphoid pools from three to ten animals were used ●, ■, ▲, ▼, Experiments where different animals from simultaneously immunized groups were sequentially followed, in these cases pools of three to five animals were used In the group of animals represented by (●----●), the mean percentage inhibition of cytolysis caused by 10^{-5} M histamine together with the s e m of triplicate assays are shown for 10, 14 and 17 d following immunization These animals are further described in Table 1

These experiments were largely performed with pooled cell suspensions obtained from three to ten similarly immunized

Table 1 *In vitro* Effects of Histamine on Cyclic AMP Levels and Cytolytic Activity of Splenic Lymphoid Cells taken at Various Times during the Primary Immune Response to Alloantigen

Days following immunization	% Specific lysis in 4 h	% Inhibition by histamine (molar)					% Increase in cyclic AMP by 10^{-5} M histamine
		10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	
10	29	8	7	8	0	0	70±37*
14	32	25	25	30	15	3	52±14
17	24	40	50	52	26	9	48±6
Non-immune	—	—	—	—	—	—	57±12

Thirty C57Bl mice were immunized with DBA/2 cells as described in Fig 1 Groups of at least six of these mice were killed on each of the days indicated and splenic lymphocytes assayed for cytolytic activity towards DBA/2 target cells and for augmentation of cyclic AMP levels in the presence of histamine Cytolysis and inhibition of cytolysis by histamine were calculated as in Fig 1 For cyclic AMP assays, 10^7 splenic cells were incubated with or without histamine in 1 ml Eagle's medium for 10 min at 37° C The cells were centrifuged, resuspended in 0 5 ml 5% trichloroacetic acid, and cyclic AMP determined All assays are based on triplicate or quadruplicate determinations

*Mean ± s e m of quadruplicate determinations These values were computed by randomly pairing values for control and histamine tubes, then taking the mean and s e m of the resulting ratios between these random pairs This method of calculation yields standard errors considerably larger than those calculated by an alternative approach (that is, computing an average for the control tubes, and calculating the standard error based on variations only in the histamine-containing tubes) animals Further studies, in which individual animals were assayed, showed the same pattern and showed very little animal to animal variability Thus, in one series of experiments (▼, Fig 1), five animals killed on day 11 and individually assayed showed an inhibition of specific cytolysis by 10^{-5} M histamine of 12±3% (s e m) while five animals from the same group tested on day 13 were inhibited 33±3% by the same histamine dosage

The alteration in the susceptibility to histamine was not related to the specific cytolytic activity of the spleen cell populations, for with any given effector cell population the percentage inhibition of specific cytolysis by histamine did not change significantly when lymphocyte/target cell ratios were varied from 200 to 1 to 30 to 1, although such alterations changed the total lytic activity about five-fold Further, when effector cells at the peak of cytolytic activity (day 11) were diluted with normal syngeneic spleen cells to give a lytic activity comparable with later (day 18) cells, the day 11 cells were still only poorly suppressed by histamine (20%), while the day 18 cells with identical cytolytic activity showed marked (43%) suppression

The variability in histamine inhibition was not due to some unique characteristic of the incubation time employed in the cytolytic assays, for the percentage inhibition of specific cytolysis caused by histamine remained constant between 1 h and 4 h after addition of histamine The increased susceptibility to histamine was likewise not due to an alteration in the threshold histamine concentration which caused inhibition, for maximal inhibition of cytolysis was in all cases observed with between 10^{-5} M and 10^{-4} M histamine (Table 1) Failure to inhibit cytolysis further with increasing concentrations of histamine suggests that the specific receptor units have been saturated at 10^{-5} M histamine

It thus seems most likely that the variation in susceptibility to histamine of different cytolytically active lymphoid cell pools relates to the number of lymphocytes bearing specific histamine receptors

In previous studies we have shown that histamine increases the cyclic AMP levels of spleen cells[9,18] If the acquisition of histamine receptors by cytolytically active lymphoid cells reflected a general change in the surface characteristics of splenic lymphocyte populations, one would expect that spleens taken from animals 17 d after immunization would exhibit *in vitro* a greater cyclic AMP response to histamine than would comparable cell populations obtained 10 d after antigen challenge Consequently, the cyclic AMP levels of spleen cell populations taken from animals at various times following immunization were measured in the presence and absence of histamine (Table 1) The cyclic AMP levels of lymphocytes taken 10, 14 and 17 d after immunization were increased to the same extent by 10^{-5} M histamine in spite of the greatly increased susceptibility to histamine of the cytolytically active cells in the same pool Similar findings have been obtained with histamine concentrations up to 10^{-3} M There is, therefore, no evidence of a general change in the proportion of histamine receptor-bearing lymphocytes in the spleen cell pools following immunization The increase in histamine receptors on effector T cells, which apparently represent only some 2–4% of the total lymphocyte population[20], was, as expected, too low to notice by cyclic AMP augmentation criteria

To ensure that the increase in histamine receptors on cytolytically active cells was a result of acquisition of receptors of the histamine 2 type, the pattern of burimamide antagonism to the histamine suppression was examined As seen in Table 2, burimamide quantitatively reversed the inhibition of cytolysis caused by histamine in a similar manner throughout the period of increasing susceptibility to histamine This burimamide effect strongly suggests that the histamine receptor which is increasing is of the histamine 2 type We have observed, however, that burimamide has less effect in reversing the histamine inhibition of cytolysis when earlier (10 d) effector cells are used

Table 2 Histamine Inhibition of Cytolysis and its Reversal by Burimamide at Various Stages of the Immune Response

Days following immunization	No of expts	% Inhibition of cytolysis by 10^{-5} M histamine	% Reversal of histamine inhibition by 10^{-4} M burimamide*
11	8	16 2 ± 2 6†	44 ± 12
13	3	28 0 ± 3 1	46 ± 1
14	8	32 5 ± 4 1	53 ± 8

* The cytolytic activity of C57Bl/6 animals immunized with DBA/2 cells was assayed, as described in text, at various times following antigenic stimulation The percentage inhibition in the presence of 10^{-5} M histamine was measured on each occasion Similarly, the effect of mixtures of 10^{-4} M burimamide and 10^{-5} M histamine on cytolysis was also measured The percentage reversal of histamine inhibition by burimamide was calculated as

$$100 \times \frac{\text{(percentage inhibition by histamine)} - \text{(percentage inhibition by histamine + burimamide)}}{\text{(percentage inhibition by histamine)}}$$

† Mean ± s e m

The immunological significance of lymphocyte sub-populations bearing histamine receptors remains to be established The recent important observations of Shearer *et al*[14] would, however, support the concept that such cells may possess an immunoregulatory function These investigators have shown that when histamine receptor-bearing cells were removed from a normal spleen cell population, the residual cells had an enhanced capacity to produce antibody to sheep erythrocytes The derivation of the lymphocyte population bearing histamine receptors was not established in Shearer's study It seems clear, however, that such receptors are not exclusively confined to thymus-derived lymphocytes[12,13] Our investigations suggest that the acquisition of histamine receptor units usually follows the differentiation of the antigen recognition unit on the effector T lymphocyte, in that specific cytolytic activity, which is dependent on antigen binding, precedes susceptibility to histamine inhibition The coincident decline of specific cytolytic activity accompanying the development of histamine receptors makes it tempting to speculate that the histamine receptor unit on effector T cells is related to immunoregulation, perhaps by providing a means of controlling T cell proliferation We are now investigating this hypothesis

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Inhibition of Histamine Release by Histamine controlled by H2 Receptor

AGENTS which increase the intracellular level of adenosine 3′-5′-monophosphate (cyclic AMP) in human leukocyte preparations such as the catecholamines, methylxanthines and prostaglandins, inhibit the antigen induced, IgE antibody mediated release of histamine from human leukocytes (basophils)[1–4]. Not only are the dose response relationships for increased cyclic AMP levels and the inhibition of histamine release similar, but the kinetics of the two events are also parallel and it is accepted as a working hypothesis that changes in the cyclic AMP level of human basophils (and mast cells) modulate the *in vitro* allergic response[4–6]. Recently, we showed that exogenous histamine could increase the cyclic AMP level of human leukocyte preparations and stop the release of endogenous histamine. This occurred at concentrations of histamine (about 10^{-6} M) which are present in the cell suspension under study[7]. For this reason we suggested that histamine could "feedback" to control the spread of an allergic response by decreasing the response of other target cells (tissue mast cells, blood basophils) to an allergenic challenge. No clear effect of antihistamines on the inhibition of histamine release by histamine was observed: concentrations up to 10^{-3} M to 10^{-4} M of several antihistamines had little effect and higher concentrations of these drugs either caused inhibition of histamine release themselves or were cytotoxic[2,7].

Ash and Schild have postulated that there are at least two types of histamine receptors. The first, inhibited by standard antihistamines, controlled the increased vasodilatation and smooth muscle contraction caused by histamine. They were designated H1 receptors. Other types of receptors probably mediated the responses not blocked by standard antihistamines, such as gastric acid secretion or the relaxation of the rat uterus[8]. Black *et al.* have validated this supposition by showing that a new drug, burimamide, antagonizes the responses to histamine which are not affected by standard antihistamines (anti-H1) without blocking the H1 receptors[9]. This drug may therefore be considered to combine with and block H2 receptors. We here report that burimamide (anti-H2) blocks the effects of histamine on leukocyte cyclic AMP levels and on the antigen-IgE antibody mediated release of histamine, whereas a standard antihistamine (anti-H1) has no effect.

Human leukocytes from donors allergic to ragweed or grass were separated from the other formed elements of the blood, washed free of serum and suspended in a serum-free Tris buffered medium containing 0.03% HSA, as described previously[10]. As histamine, in common with other agents which increase cyclic AMP, has an effect only early in the sequence of reactions leading to histamine release, it was studied in the first stage of the response[11]. The first stage is generated by exposing the cell preparations to antigen for 2 min at 37° C in the absence of calcium and magnesium and then washing the cells twice in cold buffer. This leads to a cell which is activated and will release histamine (in the second stage) when provided with antigen free buffer containing calcium and magnesium at 37° C. The activated first stage cell is stable for 30 min at 4° C (ref. 11) and the washing and resuspension of the cells take less than 10 min. In these experiments, control cell preparations were exposed to antigen under first stage conditions but the experimental cell preparations were challenged with antigen together with either histamine alone or with the drugs. In other controls, histamine and/or burimamide were studied in the second stage. They had no effect on histamine release. Histamine was measured fluorometrically as previously described[7,10,11] and cyclic AMP cells were measured by the protein binding method of Brown *et al.*[12,13] after 10 min incubation with histamine and antihistamines.

Figure 1 shows several experiments comparing the effects of burimamide and diphenylhydramine on the cells of a single donor assayed on successive days. Neither drug had an effect, at these concentrations, on the cells or on the assay of histamine. Burimamide blocked the inhibitory effect of 10^{-6} M histamine about 50% at 10^{-5} M while diphenylhydramine had no effect at this concentration. The relative effects of burimamide and diphenylhydramine were compared in several additional donors with the same result. Four such experiments are shown in Table 1. Several other types of anti-H1 drugs (tripelennamine,

Table 1 Effects of Anti-H1 (Diphenylhydramine) and Anti-H2 (Burimamide) Drugs

A, Blocking of histamine induced inhibition of histamine release

	Exp. 1		Exp. 2		Exp. 3		Exp. 4	
	% Inhibition	% Blocking	% Inhibition	% Blocking	% Inhibition	% Blocking	% Inhibition	% Blocking
Histamine, 10^{-6} M	70±2		57±6		42±3		51±3	
Histamine+aH2, 10^{-5} M	33±6	53	14±4	76	14±4	65	12±2	77
Histamine+aH1, 10^{-5} M	75±3	0	52±5	5	46±7	0	51±3	0

B, Blocking of the histamine induced increase in cyclic AMP (pmol cyclic AMP per 10^7 cells)

	Exp. 1	Exp. 2	Exp. 3	Exp. 4	Exp. 5	Exp. 6
Control	7.8±1.3	1.2±0.7	4.5±0.7	2.8±0.5	3.25±0.3	0.85±0.05
Histamine, 10^{-5} M	14.3±1.7	3.7±0.7	7.8±0.5	4.3±0.9	12.4 ±2.3	4.2 ±0.2
aH2, 10^{-4} M	5.5±1.5	2.1±1.1	6.0±0.4	2.5±0.4	—	—
Histamine+aH2	[illegible].4±0.2	1.6±0.5	4.5±0.6	3.0±0.6	—	—
aH1, 10^{-4} M	—	—	—	2.2±0.3	2.0 ±0.1	0.80±0.6
Histamine+aH1	—	—	—	5.2±0.4	11.8 ±2.2	4.0 ±0.6

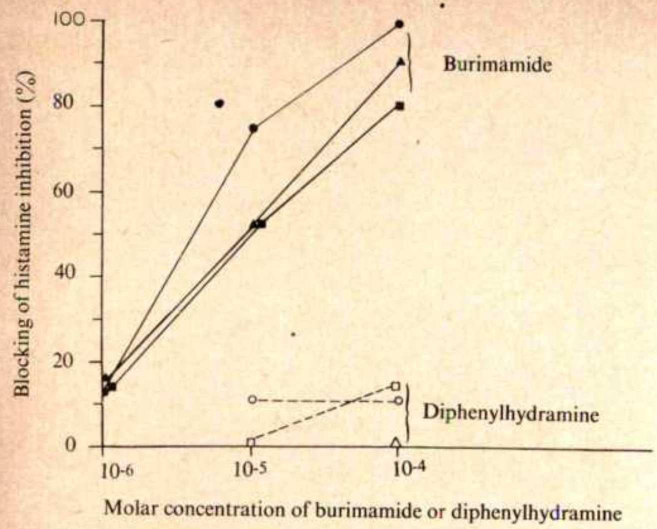

Fig. 1 Blocking of histamine inhibition of IgE mediated histamine release by burimamide and diphenylhydramine.

chlorpheniramine, pyrilamine, cyclizine and promethazine) have also been studied and, at concentrations of up to 10^{-4} M, have no blocking effect on the histamine induced inhibition of histamine release[2]. The effects of burimamide were specific and, in experiments in which it blocked the inhibitory effects of histamine, the inhibition caused by isoproterenol and prostaglandin E1 was not antagonized.

Burimamide also blocked the increased levels of leukocyte cyclic AMP caused by treatment of the cells with histamine. Six separate experiments are shown in Table 1. In all instances, the effect of 10^{-5} M histamine was blocked by 10^{-4} M burimamide. Diphenylhydramine at this concentration did not block the effect of histamine. As noted, at higher concentrations it has agonist activity and/or is cytotoxic so it could not be used in the present experiments.

These data indicate that the basophils have H2 receptors for histamine. It would seem that there are at least two receptors which mediate the action of histamine. In the context of allergic or inflammatory responses, the H1 receptor mediates the vasodilatation and increased vascular permeability which are characteristic of the response to histamine. The H2 receptor, located on the histamine releasing cells, possibly mediates an inhibitory effect on the inflammatory responses as increased cyclic AMP levels in these cells diminishes histamine release and therefore the intensity of the response. The availability of antagonists for both types of histamine receptors should allow the testing of the relative importance of these two aspects of the inflammatory response in a variety of situations.

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Inhibition and Reversal of Platelet Activation by Cytochalasin B or Colcemid

PLATELETS respond to activation by forming pseudopodia[1,2] but the relationship between pseudopodia, adhesion, spreading, and aggregation is not known, although it has been suggested that the formation of pseudopodia is an essential condition for platelet aggregation[3].

On the basis of our scanning electron microscopy (SEM) and phase contrast microscopy studies of normal platelets which we present here, we postulated that the formation of elongated pseudopodia precedes, and is necessary for, platelet spreading and aggregation. Because platelet pseudopodia contain microfilaments[4,5], we suspected that cytochalasin B (CB), a drug which disrupts microfilaments[6], would inhibit the formation of pseudopodia and would inhibit spreading and aggregation of activated platelets. CB did indeed inhibit the formation of pseudopodia and neither spreading nor aggregation occurred.

In another set of experiments, platelets that already had formed pseudopodia, spread, and aggregated, were treated with CB. After 1 h pseudopodia, spreading, and aggregation were no longer present. We suspected that platelet spreading was dependent on the circumferential band of microtubules that has been observed, just inside the surface membrane, by Hoak[7]. To test this, we used colcemid, a plant alkaloid which binds to microtubules[8]. We found that colcemid blocked membrane spreading but did not inhibit the formation of pseudopodia or platelet aggregation. Further, when platelets that had already spread were treated with colcemid, spreading was no longer present 1 h after treatment.

Plasma rich in platelets was obtained by differential centrifugation of human peripheral blood collected in

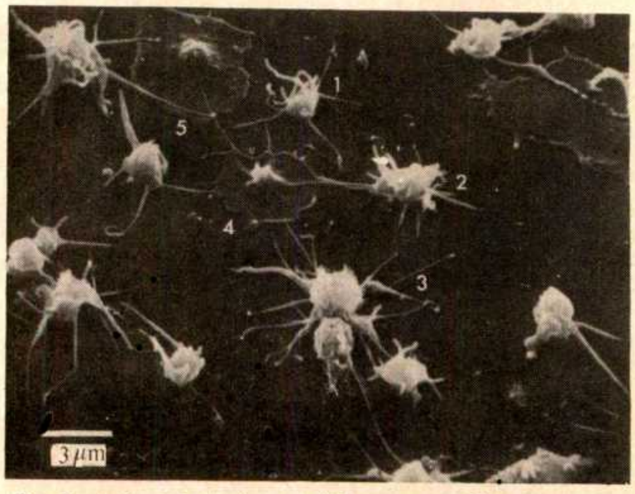

Fig. 1 Activated platelets at different stages after activation.

heparinized syringes. Cells were washed once in Dulbecco's phosphate buffered saline (PBS), resuspended in 25% donor serum and 75% PBS, and 0.1 ml of cell suspension was pipetted onto round glass coverslips. For the cytochalasin B experiments, 0.1 ml 10 $\mu g\ ml^{-1}$ cytochalasin B (ICL Research Laboratories), dissolved in 0.00001% dimethylsulphoxide (DMSO) in PBS, was added and the cells incubated at 37° C (CO_2 incubator) for 1 h. For the controls, 0.1 ml 0.00001% DMSO without cytochalasin B was added. For the colcemid experiments, 0.1 ml 10^{-6} M colcemid (GIBCO) in PBS was added and the cells incubated for 1 h. The controls had 0.1 ml PBS without colcemid. The platelets were fixed for 30 min in 1% glutaraldehyde followed by 1% osmium tetroxide. The specimens were dried by the critical point method of Cohen[9] and coated with 50–100 Å of gold in an Edwards Evaporator with a Ladd Rotary Shadower. They were examined in a Kert-Cambridge S4 Scanning Electron Microscope (SEM) operated at 20 kV. Polaroid 55 P/N film was used for the micrographs. A Zeiss phase microscope was used to view cells in both a living and dried state.

Platelets respond to activation (Fig. 1) by forming elongated pseudopodia which adhere to the substrate. After adhesion (1, 2), the pseudopodia thicken as cytoplasm flows into them (3). This continues (4) until spaces between pseudopodia are obliterated and the platelet appears as a central elevation surrounded by a "skirt" of membrane (5). This latter process of membrane flow is termed "spreading".

The aggregation of platelet involves pseudopodia which adhere to other platelets and interlock with pseudopodia of other platelets, thus forming clumps held together by a mesh of pseudopodia (Fig. 2). Usually platelets at the bottom of an aggregate are spread on the glass and the rest of the aggregate is attached to the spread platelets by pseudopodia.

Platelets treated with CB do not form elongated pseudopodia, spread, or aggregate (Fig. 3). DMSO alone does not have this effect. Colcemid treated platelets form pseudopodia and aggregate, but do not spread (Fig. 2).

Platelets that have formed pseudopodia, spread, and aggregated on glass during a 30 min preincubation are treated with CB. After a 1 h incubation, the elongated pseudopodia disappear indicating that formation of pseudopodia is reversible. No spreading or aggregation was observed. Cells preincubated for 30 min on cover slips and then treated with colcemid had pseudopodia and formed aggregates but only 3–5% showed spreading. This suggests that spreading is reversible.

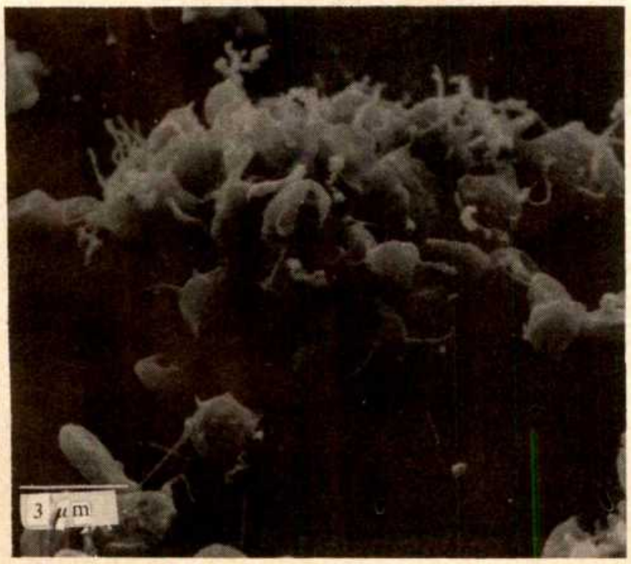

Fig. 2 Aggregate of platelets treated with colcemid.

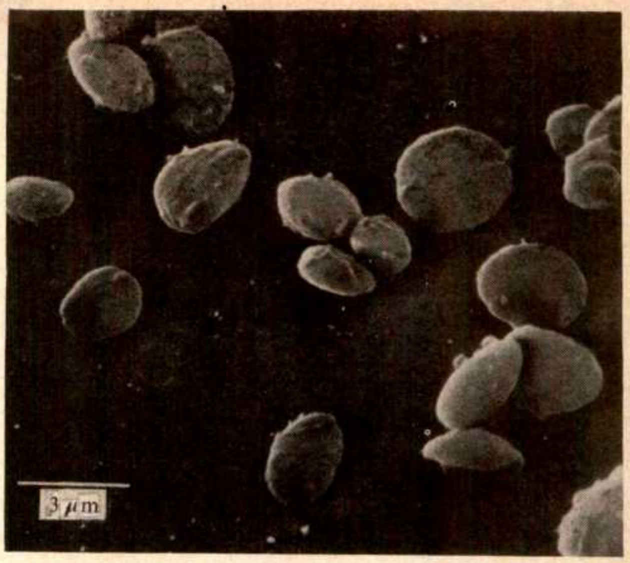

Fig. 3 Platelets treated with cytochalasin B.

These results establish that the formation of pseudopodia precedes and is essential for spreading and aggregation, that spreading is reversible and is not necessary for aggregation, and that adhesion is reversible. Platelet activation may therefore be described as occurring in three sequential stages: pseudopodia formation, adhesion, and spreading and/or aggregation. CB blocks the first step and reverses all the steps if they have occurred before the addition of CB. Colcemid blocks spreading and reverses it. These results indicate that cell to cell adhesion involves microprojections, in this case pseudopodia.

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Properties of Cystinotic Fibroblast-D98 Cell Hybrids studied by Somatic Cell Hybridization

Since the discovery of somatic cell hybridization[1] this technique has been used primarily for studies of formal genetics, cell differentiation, and cancer[2]. This study represents an attempt to use this technique to study a metabolic disease in which the primary defect is unknown.

In the nephropathic form of cystinosis, patients appear normal at birth, but by 7–8 months of age they have deficiencies in the renal tubular reabsorption of water, phosphate, sodium, potassium, bicarbonate, glucose, amino acids and other organic

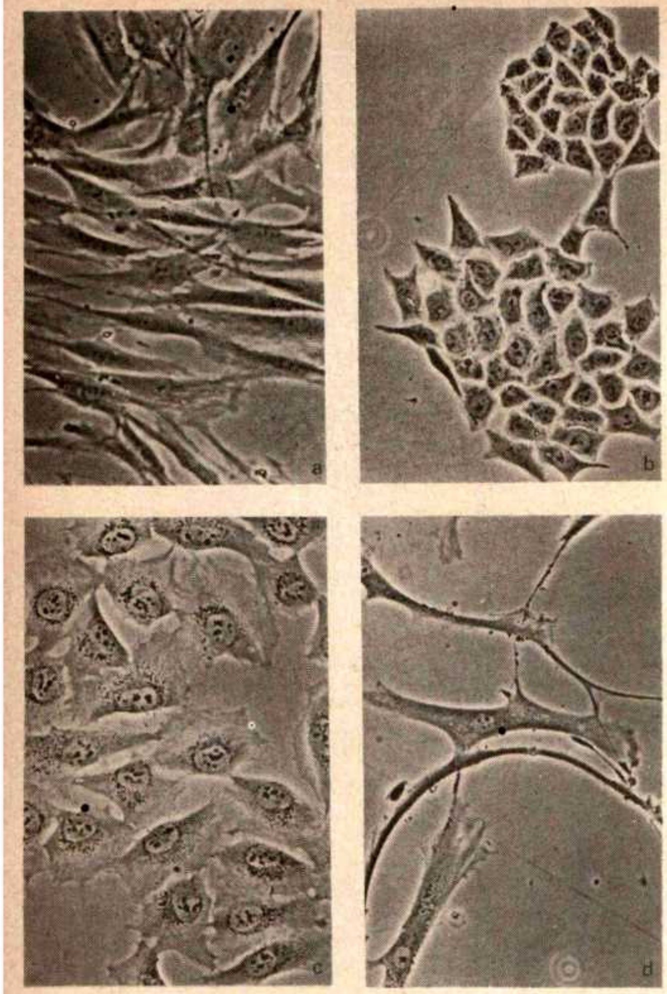

Fig. 1 The cystinotic fibroblasts were obtained from a skin biopsy of a 6-yr-old girl with nephropathic cystinosis. Cultures were maintained in Coon's modification of Ham's F12 medium and hybridization accomplished with β-propiolactone inactivated Sendai virus as previously described[19]. All cultures were checked at monthly intervals for evidence of mycoplasm contamination[22-24], which was never found. The pictures are phase contrast micrographs (×157). *a*, Cystinotic fibroblasts; *b*, D98/AH-2; *c*, clone DC 34; *d*, clone DC 26.

acids. This syndrome of tubular dysfunction is called the renal Fanconi syndrome. Although the symptoms caused by these tubular defects are usually easy to manage, children with cystinosis also have progressive glomerular damage, which leads to death from uraemia, generally before 10 yr of age. Most of the body cells in these children contain about 100 times more free (non-protein) cystine than normal. By studying either peripheral leukocytes or fibroblasts grown in culture, it has been possible to identify heterozygotes for this disease, because their cells contain approximately five times more free cystine than normal[3-5].

The discovery that the cystine in cystinotic cells is located in lysosomes[4,6,7] suggested that the metabolic defect was the absence of a lysosomal enzyme required for cystine metabolism. Attempts at identifying a lysosomal defect, however, have been unsuccessful[8]. The best explanations so far for this disease are either a specific defect of disulphide efflux at the lysosomal membrane or the lack of a reductive mechanism which may or may not be located within lysosomes.

We hoped that hybridizing a fibroblast from a child with cystinosis with a non-cystinotic cell might elucidate the metabolism of cystine in both normal and cystinotic cells[9]. Although it was not possible to predict the free cystine content of such hybrid cells, we hoped segregation would occur and the free cystine content would vary in different hybrid clones. These values might range anywhere from the small amount found in normal cells to the hundred-fold increase found in cystinotic cells. It might then be possible to correlate these differences with morphological, karyological, or biochemical differences between the hybrid clones.

D98/AH-2 (to be abbreviated D98) is a hypoxanthine-guanine phosphoribosyltransferase negative (HGPRT$^-$) derivative of human cell line Detroit 98 (obtained from the American Type Culture Collection, Rockville, Maryland), and was selected as the non-cystinotic cell in this study for six reasons. (1) D98 has a normal cystine content. (2) It is of human origin, and the likelihood of significant chromosome loss is less in intraspecific hybrids[2]. (3) Because it lacks the enzyme HGPRT it is not viable in HAT media (hypoxanthine, aminopterine and thymidine[10]), providing an easy selective system against this cell type. (4) This cell, D98, has the A isoenzyme glucose-6-phosphate dehydrogenase[11-13], providing a biochemical marker as the cystinotic cell used would have the B isoenzyme. (5) D98 has a number of marker chromosomes[14,15]. (6) It is easy to hybridize and has previously been hybridized with cells of murine[16] and human origin[17,18]. As HeLa cells also have the A isoenzyme glucose-6-phosphate dehydrogenase[11] and have marker chromosomes similar to those seen in D98[14], we assume that D98 is a derivative of HeLa cells.

Cystinotic fibroblasts and D98 cells are very different morphologically (Fig. 1*a* and *b*). The cystinotic cells have a typical fibroblastic appearance while the D98 cells are smaller, epithelial in appearance, form more compact colonies, have nuclei which appear larger relative to cell size and contain more nucleoli per nucleus. These two cell types were fused with inactivated Sendai virus by methods previously described[19]. Because only a half-selective system was used, the surviving clones included both cystinotic and hybrid clones. Thirteen hybrid clones were selected on the basis of morphology, attempting to obtain as diverse a group of clones as possible. Most clones were epithelial (Fig. 1*c*), but some were fibroblastic (Fig. 1*d*). The clones which were most epithelial also formed the most compact colonies, had the largest nuclei relative to cell size and contained the most nucleoli. Some cystinotic clones were also selected to make certain that treatment with inactivated Sendai virus and exposure to HAT medium had not changed their cystine content.

Table 1 summarizes the chromosome data. D98/AH-2 (D98) is a heteroploid cell line and has a modal chromosome number of 62. If the hybrid cells had no chromosome loss they would have a modal chromosome number of 108 (62+46). It can be estimated from the data in Table 1 that the chromosome loss in these hybrids averaged about 10%. Figure 2 is a karyotype of D98 prepared by Giemsa staining after trypsin treatment.

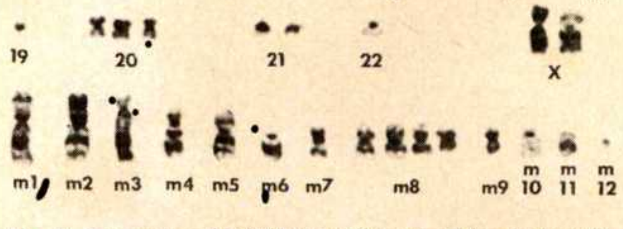

Fig. 2 Karyotype of D98/AH-2 cell prepared by the trypsin-Giemsa method. The twelve marker chromosomes are labelled m 1 to m 12.

This cell had 63 chromosomes and demonstrated twelve different marker chromosomes. Only one copy of chromosomes 3 and 5 is present. This might suggest that D98 is monosomic for these chromosomes. Closer study of the marker chromosomes showed that this was not the case as portions of chromosome 3 are seen in marker chromosomes 1 and 2, and portions of chromosome 5 are seen in markers 1, 3 and 8[15]. Figure 3 is a karyotype of hybrid clone DC 26 (see Fig. 1*d*) prepared by quinacrine mustard staining. This cell contained 101 chromosomes including one copy each of the twelve D98 marker chromosomes (but four copies of m 8). A more detailed analysis of the chromosomal findings in these hybrids will be reported elsewhere[15].

The cystinotic cell used contained the B isoenzyme G-6-PD. D98 has the faster moving A isoenzyme G-6-PD. All thirteen hybrid clones had both A and B isoenzymes (Fig. 4). When extracts from both parental cells were mixed and electrophoresed together (channel 3, Fig. 4), both the A and B isoenzymes are seen. In the hybrid clones (numbers 2 and 4, Fig. 4) a third band of G-6-PD activity is seen between the A and B isoenzymes. This strongly suggests the presence of heteropolymeric G-6-PD molecules in the hybrid cells, and provides independent evidence that the cells studied are hybrid cells. The reasoning for this is that the subunits of isoenzymes A and B of G-6-PD are not able to interchange after the complete enzyme molecule is formed, but may do so during their primary aggregation if synthesized in the same cell.

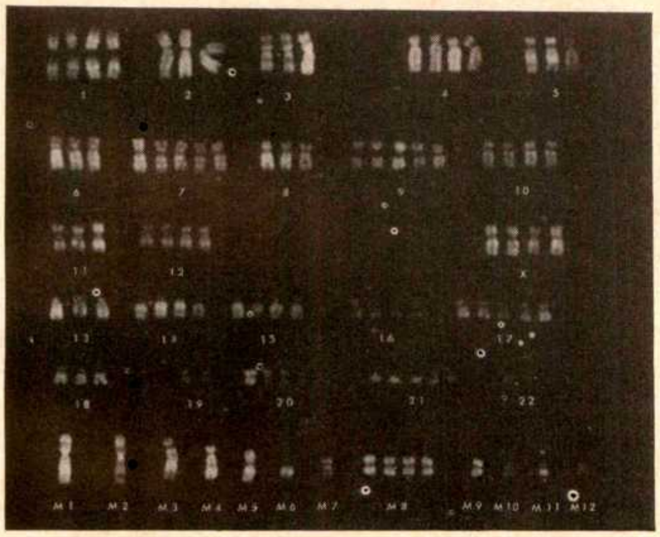

Fig. 3 Fluorescent karyotype of DC 26 cell. It shows 101 chromosomes.

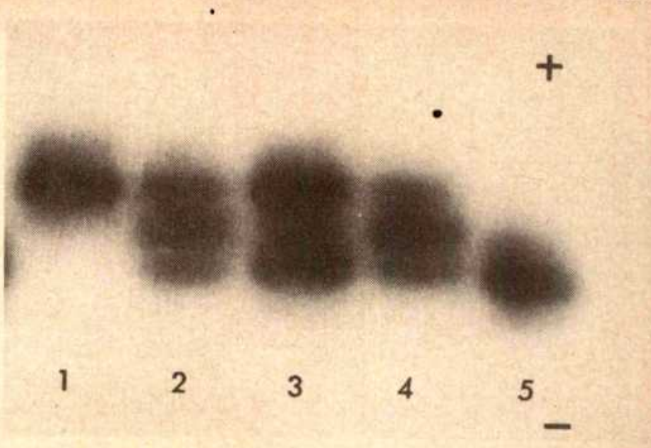

Fig. 4 Electrophoretic pattern of glucose-6-phosphate dehydrogenase (G-6-PD) using vertical starch gel electrophoresis. A Tris-EDTA-borate buffer[25] (*p*H 8.6) was used as outlined by Ruddle and Nichols[26]. NADP (10 mg) was added to the gel before degassing and to the cathode buffer. Starch gels were run at 0-4° C for 20 h at 7.5 V cm^{-1} within the gel and approximately 15 mA and were then stained with MTT tetrazolium and phenazine methosulphate. Channel 1 represents parental cell D98; channel 2 represents hybrid clone DC 34; channel 3 represents a mixture of extracts from D98 cells and cystinotic fibroblasts; channel 4 represents hybrid clone DC 26; channel 5 represents cystinotic fibroblasts.

The free (non-protein) cystine content of the hybrid clones is outlined in Table 2. It can be seen that the free cystine content was in the normal range in each hybrid clone studied.

The free cystine content of the hybrid clones is somewhat less than that of the D98 (that is, normal parent) when expressed as nmol half cystine per mg protein. The protein content of a D98 cell is about half that of a hybrid cell, however, and therefore the free cystine content per cell is very similar in the hybrid clones as compared with D98. C-0 is the cystinotic cell before fusion and C-1 is a cystinotic clone which was selected after treatment with inactivated Sendai virus and HAT medium.

Table 1 Karyology of Parent and Hybrid Clones

	No. of metaphases in each range of chromosome counts									
"Parent" cells	<46	46	47-54	55-66	67-80	81-91	92-100	101-112	>112	Total counted
D98			1	17		2		2		22
Cystinotic fibroblast	1	9								10
Hybrid cells										
Expected								*		
DC 11					1	3	10			14
DC 14							3	2		5
DC 20						3	5	4		12
DC 22						2	10			12
DC 23					1	5	3	4	2	15
DC 24							12		2	14
DC 26						1	6	8		15
DC 30	1			1		2	5	4	2	15
DC 31						6	8	6	2	22
DC 33							3	4		7
DC 34						1	5	22		28
DC 35A				2		1		6		9
DC 37						1	5	3	1	10

Chromosome preparations and biochemical studies were done within 20-35 generations after the formation of hybrid cells. The cells were treated with colcemid (Grand Island Biological Co., 1×10^{-6} M) for 2-4 h before collection and exposed to 0.075 M KCl for 8 min and fixed in methanol: acetic acid (3:1). The slides were air dried. Quinacrine mustard staining and fluorescent photomicroscopy were performed as described by Caspersson *et al.*[20]. For demonstration of Giemsa bands, well-dried slides were dipped into 0.2% trypsin solution (Difco Bactotrypsin in isotonic saline) for 15-30 s, rinsed briefly in isotonic saline and stained with Giemsa (Gurr, *p*H 7.0) for 5-15 min in a modification of the method described by Seabright[21].

Table 2 Free Cystine Content of Parent and Hybrid Clones

"Parent" cells	(nmol 1/2 cystine mg^{-1} protein)
D98	0.11
Cystinotic fibroblasts	
C-0	6.78
C-1	6.05
Hybrid cells	
DC 11	0.02
DC 14	0.04
DC 20	<0.01
DC 22	0.04
DC 23	0.08
DC 24	0.03
DC 26	0.01
DC 30	0.01
DC 31	0.11
DC 33	0.06
DC 34	0.03
DC 35A	0.09
DC 37	<0.01
Mean	0.04

Free cystine was measured as previously described[6].

The high cystine content of C-1 indicates that the low cystine content in the hybrid clones did not result from these procedures.

Interpretation of these data is difficult. The question to be answered is why none of the hybrid clones was similar to heterozygote cells in its cystine content. The heterozygote cell receives one normal and one abnormal gene and has a cystine content five times greater than normal. The hybrid cell receives two abnormal genes and at least two normal genes and has a normal content of free cystine. Perhaps two normal genes per cell is sufficient even if the cell is very large. Another possibility is that the heteroploid (tumour) cell has taken over "control" of the hybrid cell and that this "control" includes regulation of cystine metabolism.

One further possibility is that the D98 cell makes a substance which can reduce cystine to cysteine in the cystinotic lysosome and thus correct the defect. We are presently pursuing this possibility.

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Griseofulvin inhibits Fungal Mitosis

Griseofulvin is an antifungal antibiotic widely used for the treatment of human and animal dermatophytic infections. The *in vivo* antifungal activity of griseofulvin is a reflexion of its peculiar pharmacological properties for, after oral administration, it is specifically localized and concentrated in the keratinized cells of the skin, hair and nails. The invasive growth of dermatophytes parasitizing these tissues is inhibited and the infected tissue is removed by desquamation and the growth of new epidermal layers. Here we report the effects of griseofulvin on fungal mitosis.

Basidiobolus ranarum was used. This has one very large nucleus (25 μm long) in each hyphal compartment (Fig. 1). After mitosis, the daughter nuclei move rapidly apart and the compartment is divided by the centripetal growth of a septum which has no central pore. Thus, each hyphal compartment may be regarded as a single uninucleate cell. *B. ranarum* was grown at 30° C in Petri dishes containing 20 ml of a malt extract, yeast extract, glucose, peptone agar medium. The peripheral hyphae

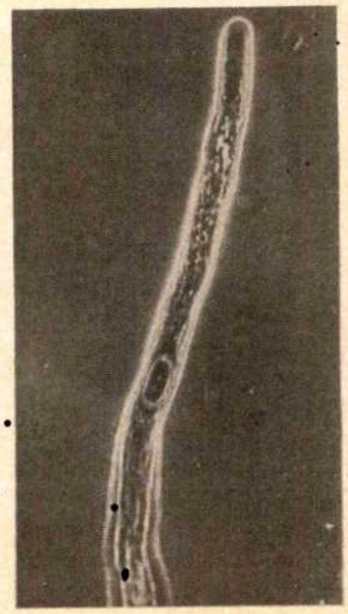


Fig. 1 Phase contrast micrograph of a normal *Basidiobolus* hypha. The large nucleus and nucleolus are easily seen.

of colonies were stained with 0.2% (w/v) aqueous acridine orange for 1 min, washed with water and examined by ultraviolet microscopy. The nucleolus fluoresced red and the condensed mitotic chromosomes fluoresced green. This technique facilitated the recognition of the various stages in mitosis.

A large proportion of hyphae growing on media containing 5 to 10 μg ml^{-1} griseofulvin had compartments which contained more than one nucleus (Figs 2 and 3). Of these multinucleate compartments 88% were binucleate, 9% were trinucleate and 3% were quadrinucleate. The multinucleate condition of many griseofulvin treated hyphae was clearly seen after acridine staining (Fig. 3). In these multinucleate hyphal compartments the nuclear membrane of each nucleus was apparent, showing that each nucleus was physically isolated from the other, even though they were very close together. Control hyphal compartments with two nuclei were seen only very rarely, and if such a cell was seen the two nuclei were always some distance apart. Control hyphal compartments with three or four nuclei were never seen. The presence of multinucleate compartments in griseofulvin treated fungi may explain the previously observed increase in their DNA content relative to controls[1].

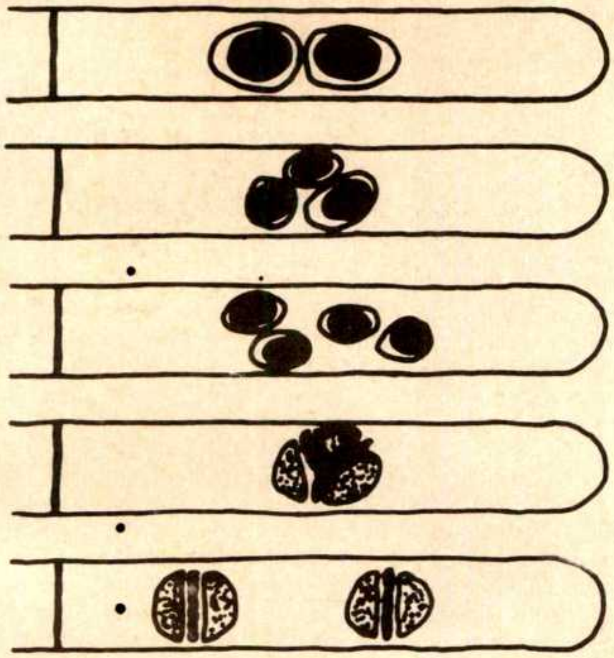


Fig. 2 Illustration of the nuclear abnormalities seen in griseofulvin treated hyphae. Hyphal compartments with two, three or four nuclei were often seen. The Y shaped metaphase often encountered is shown.

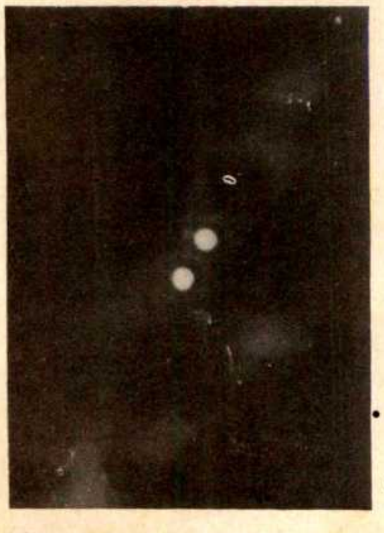
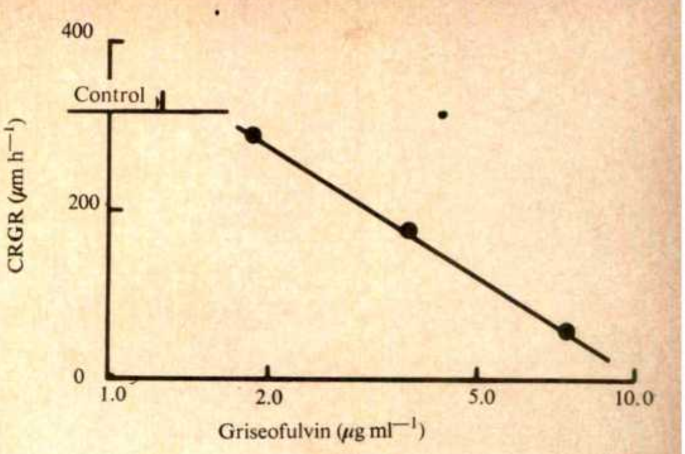


Fig. 3 A micrograph of a binucleate hyphal compartment produced by growth of *Basidiobolus* on a medium containing 5 μg ml^{-1} griseofulvin. The micrograph is of material fluorescing after staining with acridine orange. Note the brightly fluorescent nucleoli, the nuclear membranes and the close proximity of the nuclei.



Griseofulvin (μg ml^{-1})	Mitotic index
control	2.4
1.9	4.4
3.75	9.1
7.5	11.3

Fig. 4 The effect of griseofulvin on the colony radial growth rate (CRGR) and mitotic index of *Basidiobolus*. For growth rate experiments increasing concentrations of griseofulvin were incorporated into solid medium and the radial growth rate of colonies measured as previously reported[2]. Mitotic index counts were performed on parallel colonies growing on medium containing griseofulvin. Peripheral mycelium was stained in acridine orange and viewed using ultraviolet illumination on a Zeiss Universal microscope. Mitotic cells were easily seen. 1,000 to 3,000 cells were scanned and those in mitosis were classified into the various mitotic phases.

Griseofulvin also caused abnormal metaphase configurations, the most usual aberration being a Y shaped metaphase plate (Fig. 2). Occasionally, a griseofulvin treated compartment contained two nuclei which were both in mitosis (Fig. 2). The radial growth rate of *B. ranarum* colonies was inversely related to the logarithm of the griseofulvin concentration in the medium[2] (Fig. 4). There was, however, a direct relationship between the mitotic index of the mycelium and the griseofulvin concentration (Fig. 4). The known mitotic inhibitors, vinblastine, sodium cacodylate and isopropyl-N-phenyl carbamate (IPC) cause similar effects to griseofulvin on the colony radial growth rate and mitotic index of *B. ranarum*. Neither the colony radial growth rate nor the mitotic index of *B. ranarum* was affected by colchicine or 1,4-dichlorobenzene (two other inhibitors of mitosis). Inhibitors of RNA, DNA and protein synthesis, cell permeability and respiration all caused a reduction in both the colony radial growth rate and the mitotic index of *B. ranarum* (K. G. and A. P. J. T., unpublished). The observed increase in the mitotic index caused by griseofulvin and other mitotic inhibitors was not, therefore, a general response to inhibition of growth.

The number of nuclei in each phase of mitosis was calculated as a percentage of the total number of cells in the population. When these results are plotted as a histogram, a pattern emerges for the treated cells that reflects the point, or points, in the mitotic cycle where the inhibitor has most effect. We have called this histogram a plot of "Phase Accumulation Data". The terms prophase, metaphase, anaphase and telophase are applied to

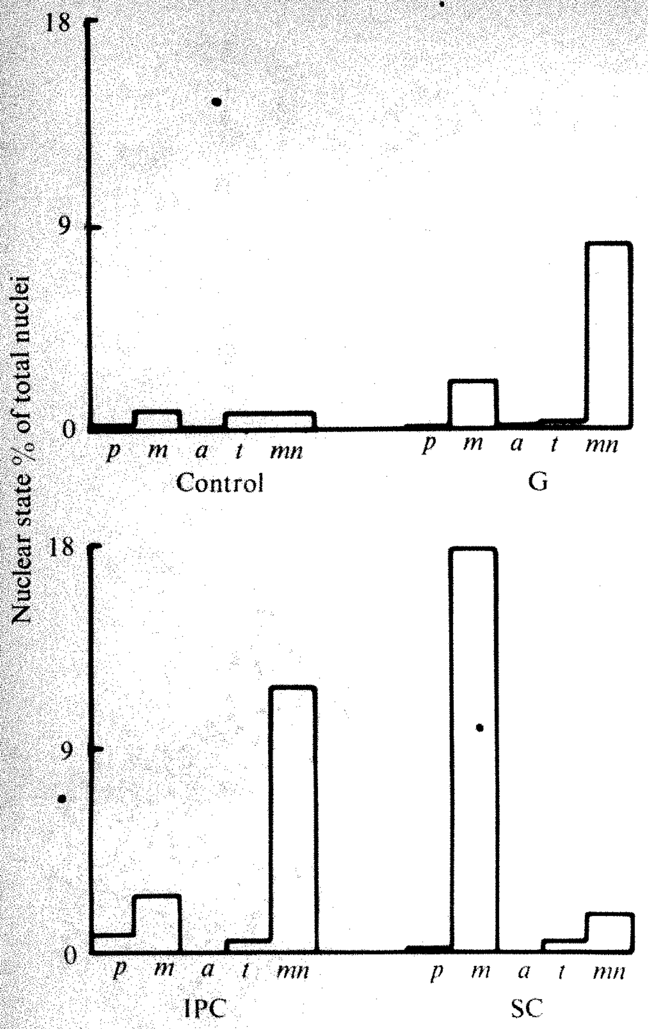


Fig. 5 Phase accumulation data for control colonies and colonies growing on mitotic inhibitors, *p*, prophase, *m*, metaphase, *a*, anaphase, *t*, telophase, and *mn*, multinucleate. The pattern for sodium cacodylate shows the block of mitosis at metaphase. The patterns for griseofulvin (G) and isopropyl-*n*-phenylcarbamate (IPC) are similar but differ from that of sodium cacodylate (SC). Griseofulvin and IPC increase the number of metaphase nuclei but they also produce large numbers of multinucleate hyphal compartments.

nuclear division in a classical manner. We have used a further term, multinucleate, to indicate a cell containing two or more nuclei each with an interphase appearance. The phase accumulation data, for all the mitosis inhibitors tested, fell into two groups, typified by sodium cacodylate and IPC (Fig. 5). Sodium cacodylate showed a colchicine-like effect in blocking large numbers of cells at metaphase and few multinucleate cells were seen. IPC, however, showed a significant peak at metaphase and very large numbers of multinucleate cells. Figure 5 shows how the phase accumulation data for griseofulvin closely resemble those of IPC but are very different from those of sodium cacodylate.

The nuclei of griseofulvin induced multinucleate compartments were always observed in close proximity (Fig. 3). In such cells the daughter nuclei appeared to move only a very short distance apart after metaphase and then reverted to the early interphase state by re-enclosure in the nuclear envelope. In this sort of situation griseofulvin may act by inhibiting the postulated sliding of microtubules[3].

IPC is known to produce disorganization of spindle microtubules in dividing plant cells[4]. Our ultrastructural observations on *Basidiobolus* have shown that griseofulvin produces very similar effects (K. G. and A. P. J. T., unpublished). There is an increasing amount of evidence suggesting that griseofulvin affects microtubules in systems other than fungal hyphae[5–8]. The ability of griseofulvin to block mitosis, in a manner differing from that of colchicine, should lead to its use as a valuable research antibiotic.

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Antimitotic Action of Griseofulvin does not Involve Disruption of Microtubules

THE antimitotic action of griseofulvin in plant and mammalian cells has been attributed to a colchicine-like disruption of microtubules. Treatment of *Vicia faba, Allium* root tips or HeLa cells with griseofulvin, for example, resulted in the accumulation of cells at metaphase[1–3]. The griseofulvin-inhibited cells contained abnormal arrays of chromosomes, identical to those produced by treatment of dividing cells with colchicine. Using polarization microscopy, Malawista *et al.*[4] found that the addition of 10^{-5} M griseofulvin to dividing *Pectinaria* oocytes reduced the size of the meiotic spindles, as measured by loss of birefringence. This action was considerably more rapid than with either podophyllotoxin or vinblastine sulphate ; moreover, on removal of the griseofulvin, recovery of the spindle also occurred much more rapidly[4]. Recent evidence indicates that several of the drugs which arrest metaphase interfere with microtubule function through different mechanisms. Colchicine and the vinca alkaloids, for example, bind to tubulin (microtubule protein) at different molecular sites[5,6]. Griseofulvin does not prevent the binding of colchicine to tubulin, nor does it affect the ability of the vinca alkaloids to stabilize the colchicine binding activity of tubulin[5]. This suggests that griseofulvin does not bind at either the colchicine or vinca alkaloid binding sites.

It is now possible to polymerize microtubules *in vitro*, in crude supernatant fractions of brain containing tubulin, by removal of calcium ions by chelation with ethylene bis(oxyethylene-nitrite) tetraacetate (EGTA)[7,8]. We studied the effect of griseofulvin on this, and found that microtubule polymerization *in vitro* was not prevented. Examination of griseofulvin-inhibited HeLa cells by electron microscopy showed morphologically normal but disoriented microtubules.

Incubation of the crude 30,000*g* supernatant brain extract containing EGTA at 37° C resulted in the formation of 250 Å diameter microtubules. Addition of 5×10^{-5} M colchicine, 2×10^{-5} M podophyllotoxin, and 2×10^{-5} M vinblastine sulphate or vincristine sulphate immediately before initiation of the polymerization reaction completely prevented microtubule formation. Polymerization *in vitro*, however, was not affected by the presence of griseofulvin (Fig. 1). At the highest griseofulvin concentration tested, 6×10^{-5} M, the microtubules formed were indistinguishable from those found in untreated samples, and the degree of microtubule formation did not seem to differ significantly.

Inhibition of multiplication of HeLa cells by griseofulvin was concentration-dependent, 50% inhibition being obtained at 4×10^{-5} M griseofulvin, and this concentration producing a mitotic index (c-mitotic cells) of 48% after 30 h of growth (data not shown). Examination of the cells, inhibited in metaphase, showed normal microtubules (Fig. 2). There seemed to be both pole-to-pole and chromosomal microtubules; the latter inserted in the usual manner into the kinetochore, and their numbers were estimated to fall into the normal range. The mitotic centres were of normal appearance, except that there was an occasional increase in the number of small vesicles in the vicinity of the centrioles. The centrioles also showed the usual morphological appearance, and were confined to the mitotic centres. An increase in mitotic centres, however, each containing two centrioles, was observed in many of the drug-treated cells, a finding which may explain the multipolar mitotic patterns observed with the light microscope[2,3]. The numerous cells found in incomplete mitosis showed mitotic arrest in or after metaphase; subhaploid numbers of chromosomes were often found in close apposition to a mitotic centre (Fig. 2). The number of chromosomes associated with any one of the multipolar mitotic centres seemed to be random. HeLa cells, treated with 2×10^{-6} M colchicine or 2×10^{-5} M podophyllotoxin, were arrested at metaphase, and, in contrast to the findings with griseofulvin-inhibited cells, they did not contain microtubules.

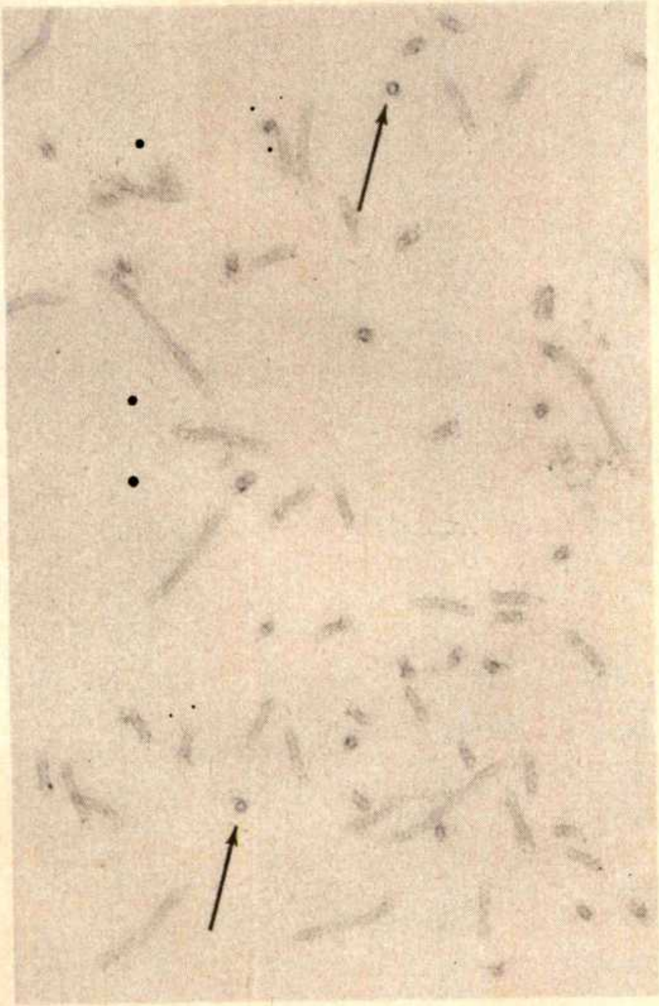

Fig. 1 Microtubules polymerized *in vitro* in the presence of griseofulvin (6×10^{-5} M). The arrows point at cross-sectioned microtubules or 250 Å diameter. *In vitro* polymerization was carried out with 30,000*g* supernatant extracts of sonicated 13 to 17-d-old chick embryo brains in 20 mM sodium phosphate, 100 mM sodium glutamate, *p*H 6.75. Extracts contained 0.5 mg ml^{-1} of tubulin, 1 mM $MgCl_2$, 1 mM GTP, and 10 mM EGTA. Polymerization was initiated by raising the temperature from 0° to 37° C. The reaction was carried out for 30–60 min. Polymerized microtubules were fixed as a suspension with prewarmed (37° C) buffered 2% glutaraldehyde[11]. Microtubules were pelleted by centrifugation (10,000*g*, 30 min), then postfixed in 1% OsO_4, and embedded in 'Maraglas' by standard procedures[12,13]. Ultrathin sections were stained with uranyl and lead salts[14,15]. Magnification: ×70,000.

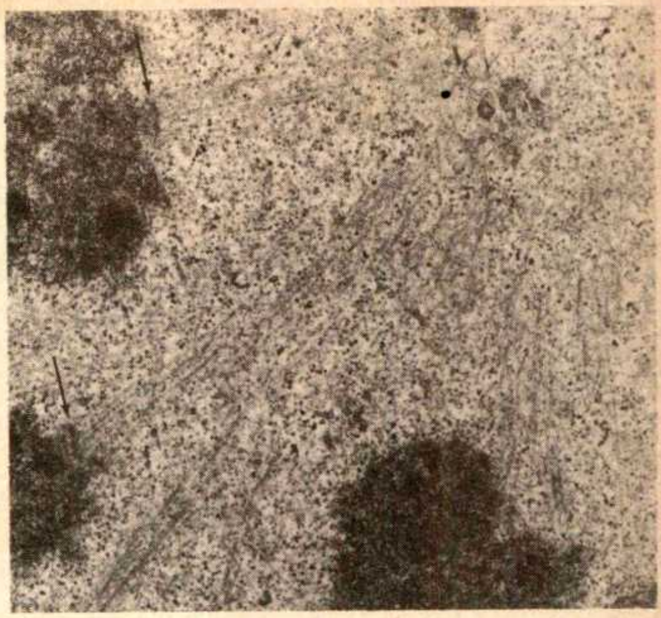

Fig. 2 Section of a HeLa cell blocked in mitosis by exposure to 2×10^{-5} M griseofulvin for 24 h. Normal microtubules radiate from a mitotic centre which occupies the right upper quadrant of the illustration to and past chromosomes. Note the normal attachment of the microtubules to kinetochores (arrows). HeLa' monolayer cultures were maintained as described previously[16]. The griseofulvin was dissolved in dimethylsulphoxide (DMSO) so that all cultures (control, griseofulvin, podophyllotoxin, and colchicine-treated) contained final DMSO concentration of 0.1%. Cell growth was not affected by the DMSO. After treatment with the drugs for 6, 12, 24, or 30 h, cells were collected by scraping them off the glass in calcium- and magnesium-free balanced salt solution containing 0.02% EDTA, and mitotic indices and cell numbers were determined. Control and treated cells utilized for electron microscopy were fixed and processed as in Fig. 1. Magnification: ×27,500.

Thus, although the action of griseofulvin on mitosis resembles that of other c-mitotic agents such as colchicine, podophyllotoxin, and the vinca alkaloids in a number of ways, it differs in that microtubule assembly is not affected. Griseofulvin shows an effect on mammalian cell mitosis which resembles that of the herbicide isopropyl-*n*-phenylcarbamate (IPC) in plant cells. Treatment of *Hemanthus katherinae* endosperm with IPC resulted in loss of spindle birefringence, and formation of multipolar spindles, and electron microscopy revealed the presence of normal but disoriented microtubules[9]. As with griseofulvin, the microtubules were associated with the kinetochores in a normal fashion (*Hemanthus* does not contain centrioles). Significant differences in the mechanisms of action of these two agents must exist, however, because IPC was found to be totally ineffective in producing mitotic arrest in HeLa cells, even at 10^{-4} M.

How does griseofulvin inhibit mitosis? Although the drug does not affect the assembly of microtubules, it may affect some aspect of microtubule function, possibly a process vital to the sliding of microtubules, which has been proposed to be necessary for separation of chromosomes[10]. Alternatively griseofulvin may not affect microtubules directly, but may act on other processes essential for normal completion of cell division. Further understanding of the mechanism of action of griseofulvin on mitosis may provide new insight into the process of cell division in eukaryotic cells.

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Quantitative Response to Daylength during Diapause in Insects

WITH few exceptions investigations into photoperiodically controlled seasonal activity in insects have used stationary light-dark cycles; no experiments known to us have defined the role of increasing or decreasing daylengths in nature. We therefore investigated the influence of natural daylengths on diapause duration and termination, using the green lacewing, *Chrysopa carnea* Stephens (Neuroptera). This species undergoes a reproductive diapause when subjected to short daylengths below a critical photoperiod[1]. A large decrease in stationary daylength above the critical photoperiod can also induce diapause; an increase in stationary daylength below the critical photoperiod can either avert or terminate diapause[2]. It was not clear from these laboratory experiments, however, if *C. carnea* can perceive natural changes in daylength, so we tested (*a*) whether the naturally decreasing daylengths in autumn have a role in maintaining diapause and (*b*) whether increasing daylengths after the winter solstice hasten the end of diapause.

To answer the first question we reared *C. carnea* outdoors in Ithaca, NY (42° 27″ N). On October 25, approximately three weeks after the animals had reached the full depth of diapause[3], we transferred samples from this overwintering population into seven photoperiodic conditions: six with stationary daylengths and one under natural illumination in a heated greenhouse. The animals remained under their respective regimes and were examined daily until diapause ended[3] and reproduction began.

The results (curve *A*, Fig. 1) show (*a*) that at photoperiods of 13 h or less there is an inverse, linear relationship between diapause duration and photoperiod, and (*b*) that when the diapause duration of the greenhouse sample (75 d) is plotted against photoperiod (arrow, curve *A*), a 9.5 h photoperiod is read on the abscissa. As this daylength is equivalent to the shortest day of the year at our latitude, it seems that the *C. carnea* perceived and responded to the duration of natural daylengths occurring through autumn and early winter. Thus, as the autumn days became shorter, between the sample date and the winter solstice, the rate of diapause development[4] slowed. Although, in the laboratory, *C. carnea* is capable of responding to decrease in daylength *per se*, our data here (curve *A*) indicate that the animals responded quantitatively to the absolute duration of autumn and early winter daylengths. These experiments are the first to demonstrate a quantitative relationship between diapause duration and daylength. In other species it has been shown that the rate of morphogenesis is quantitatively related to photoperiod[5-7] and that natural photoperiods may maintain diapause longer than a single stationary short daylength[8].

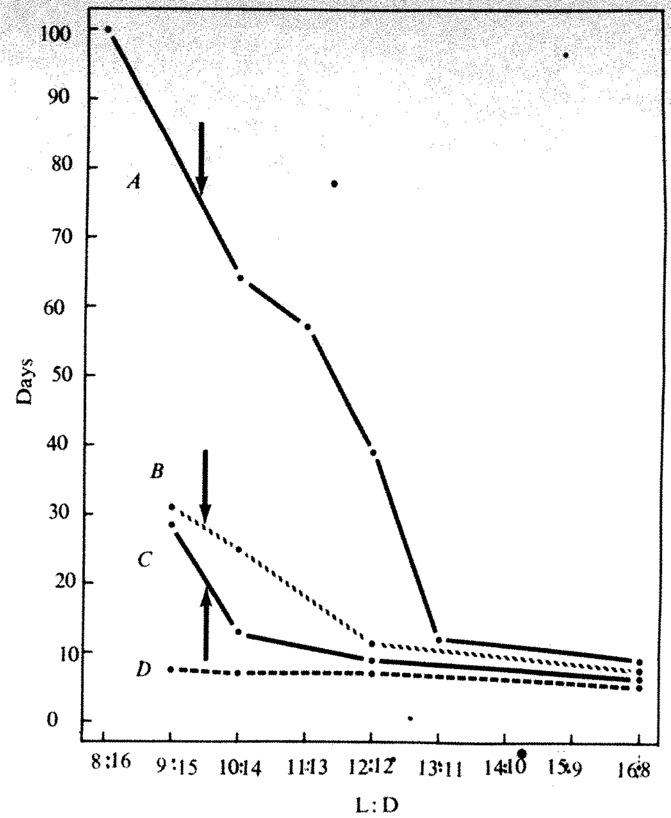

Fig. 1 Response (mean number of days to initiate oviposition) after overwintering *Chrysopa carnea* adults were transferred to various photoperiods. Sample dates: *A*, October 25, 1971; *B*, December 22, 1971; *C*, January 22, 1972; *D*, February 23, 1972. Arrows, results obtained from groups transferred to the greenhouse on the *A*, *B* and *C* sampling dates. $\bar{x}$ ± s.d., sample no. in parentheses: curve *A*——99.2±27.8 (8), 64.0±9.2 (10), 57.0±10.9 (10), 39.1±10.1 (12), 11.5±1.5 (8), 9.0±0.5 (6), greenhouse (arrow) 75.3±9.4 (12); curve *B*——30.7±6.5 (10), 25.2 ±1.5 (8), 12.4±2.3 (6), 8.3±0.7 (6), greenhouse (arrow) 27.7 ±3.3 (8); curve *C*——28.6±10.2 (12), 13.1±7.3 (12), 8.8±0.8 (10), 6.6±0.7 (6), greenhouse (arrow) 20.0±8.4 (10); curve *D* ——7.6±0.9 (10), 7.0±1.5 (10), 6.6±2.4 (10), 5.8±0.8 (10). Temperatures: incubators 24°±1° C; greenhouse 23°±4° C.

Our earlier results have shown that an abrupt increase in daylength, below the critical photoperiod, will break diapause in *C. carnea* in the laboratory[2] and that chilling does not accelerate diapause development[3]. To determine whether diapause in this species is terminated by increasing daylengths in nature, we sampled an outdoor diapausing population at the winter solstice and twice afterwards. We transferred samples into various stationary photoperiods and into a heated greenhouse under natural illumination. Our data (Fig. 1) show that within each sample period the various stationary photoperiods produced different responses. Also, the changes in the slopes of curves *A*, *B*, *C*, and *D* indicate that diapause in *C. carnea* is a dynamic state. Between January 22 (curve *C*) and February 23 (curve *D*) the response curve flattened out at 6 to 8 d, signifying that diapause had ended in nature during this period.

As diapause in the greenhouse samples (arrows on curves *A*, *B*, and *C*, Fig. 1) persisted as though the animals responded to a stationary photoperiod of approximately 9.5 h of light d^{-1}, we conclude that increasing daylengths after the winter solstice did not accelerate diapause development. Thus, increasing daylengths in nature do not terminate diapause in this species.

Studies attempting to define the role of changing daylengths on diapause fall into three categories: (*a*) in some species it is not important whether photoperiods increase, decrease, or remain stationary, the only significant factor is whether daylengths are longer or shorter than the critical photoperiod[9]; (*b*) some species require a change in daylength which crosses a critical photoperiod to evoke diapause, for example, the long-day short-day effect[10,11]; (*c*) it seems that some species respond to changes in daylength which do not cross a critical photoperiod. For example, Corbet's experiments[12] suggested that diapause is averted when photoperiods increased by more than a certain increment. Blake[13,14] infers that decreasing daylengths inhibit pupation, but she did not test the effect of stationary short daylengths. Recently, Vepsalainen[15] claimed that increasing daylengths avert diapause; his results remain inconclusive because he lacked data from a stationary long day condition for comparison. Our earlier laboratory studies[2] demonstrated that *C. carnea* can respond to the direction of change in daylengths (both increasing and decreasing) which do not cross the critical photoperiod. Our present results, however, show that in nature it is the absolute duration of the decreasing autumn daylengths which prolongs diapause in this insect. This raises the question whether the insect's photoperiodic clock detects day-to-day differences in absolute daylength or whether it detects larger differences occurring over longer periods.

Our results with *C. carnea* show that natural autumn-winter daylengths may influence diapause induction[3] and play an important role in diapause maintenance, but that after the winter solstice natural photoperiods do not terminate diapause. In view of these findings (also see Danilevsky *et al.*[16]), many laboratory studies of insect dormancy should be re-evaluated, and future studies of diapause induction, maintenance, and termination should take into account the dynamic aspects of dormancy.

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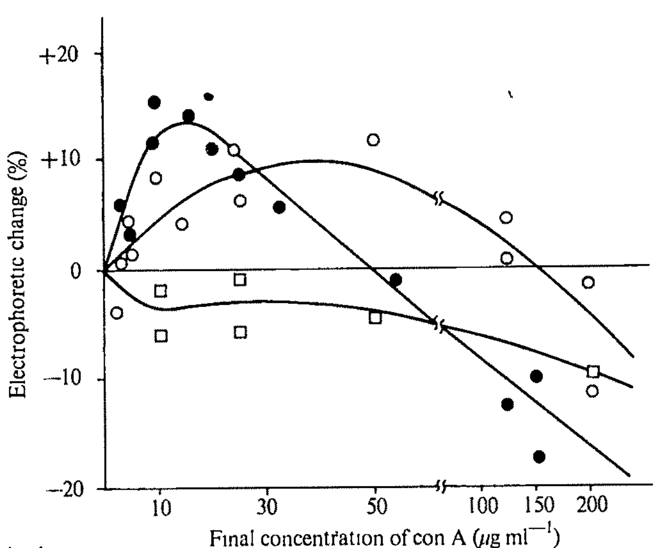
Changes in Distribution of Electric Charges in the Surface Membrane of Rat Ascites Hepatocarcinoma Cells induced by Con A

SEVERAL kinds of agglutinins of plant origin, such as concanavalin A (con A) or wheat germ agglutinin, agglutinate malignant transformed cells by interacting with specific sites on the surface membrane but only agglutinate normal parent cells after they have been treated with proteolytic enzymes such as trypsin[1-3]. As malignant transformed cells and normal cells bind almost equal amounts of agglutinins[4,5], it has been hypothesized that an increase in susceptibility to the effect of agglutinins may be due to changes in the cell surface such as a redistribution of binding sites[6] or alterations to the thickness of cell coat material[7], rather than a simple unmasking of "cryptic" receptor sites[3,8]. Cell electrophoresis is a suitable method for the detection of minimal changes to the cell surface[9,10]. Here, we describe the use of cell electrophoresis to determine whether or not any specific changes in the surface of tumour cells associated with agglutination can be induced by the action of con A.

Rat regenerating liver cells and ascites hepatocarcinoma cells (AH 62F and AH 66F)[11] were chosen as representative of normal and malignant cells respectively. One millilitre of cell suspension (2×10^6 cells) was mixed with an equal volume of one of various concentrations of con A suspended in physiological saline and was then incubated at 37° C for 10 min (standard condition of contact). The degree of agglutination was determined both macro- and microscopically. After exposure to con A, without further washing, the cells were injected through a polyethylene tube into the visual field of the electrophoretic chamber which had previously been filled with isotonic veronal buffer solution (*p*H 7.0, ionic strength 0.173). Cell electrophoretic mobilities were determined at 25±0.2° C, using the conventional cylindrical chamber described by Bangham *et al.*[12] Mobilities of twenty or more cells were measured for each sample and a comparison of the mean values between samples was made.

Figure 1 shows that con A induced biphasic changes in the electrophoretic mobility of both of the two strains of rat ascites hepatocarcinoma cells used. Low concentrations of con A (5–40 μg ml^{-1}) increased mobility whereas high concentrations (100–300 μg ml^{-1}) decreased mobility. Both the magnitude of increase in mobility and the concentration of con A needed to cause a decrease in mobility were very different for the two strains of rat ascites hepatocarcinoma studied. Agglutination of cells occurred when concentrations of con A sufficient to facilitate a decrease in mobility were used. These biphasic changes in mobility were scarcely observed when regenerating liver cells were mixed with various concentrations of con A. In this instance a decrease in mobility alone was observed. The biphasic response of mobility took place after tumour cells had been incubated either at 37° C or 4° C for 10 min. Agglutination, however, did not occur at the latter temperature[13]. There was evidence that the biphasic response of the mobility of tumour cells was induced by specific adsorption of con A onto the cell surface. It was completed within several minutes of exposure and remained constant for a further hour. No response was induced by con A which had been previously inactivated by heating at 100° C for 5 min. The response of mobility to the action of con A was reversed by competition with either α-methyl-D-glucopyranoside or D-mannose[14], when added either before or after exposure of tumour cells to con A. For example, the mobility of AH 66F cells had been decreased by 150 μg ml^{-1} of con A as much as 11%, whereas the response was completely reversed by further



Agglutination							
AH66F	–	–	±	+	++	++	+++
AH62F	–	–	–	–	±	+	++
Liver	–	–	–	–	–	–	–

Fig. 1 Changes in cell electrophoretic mobility induced by con A Two strains of rat ascites hepatocarcinoma cells, AH 66F and AH 62F, were collected from the peritoneal cavities of rats at various intervals during the exponential stage of growth after intraperitoneal inoculation of 10^7 cells The regenerating liver was collected about 48 h after removing two-thirds of the liver under anaesthesia and individual cells from the liver were obtained by mechanical separation with fine scissors and gentle homogenizing with a loosely fitting 'Teflon' homogenizer The cells were suspended in physiological saline Cell electrophoretic mobilities and agglutination were examined after exposure of cells to con A under the "standard condition of contact" The degree of agglutination was scored – to +++ (●), AH 66F, (○), AH 62F, (□), regenerating liver cells

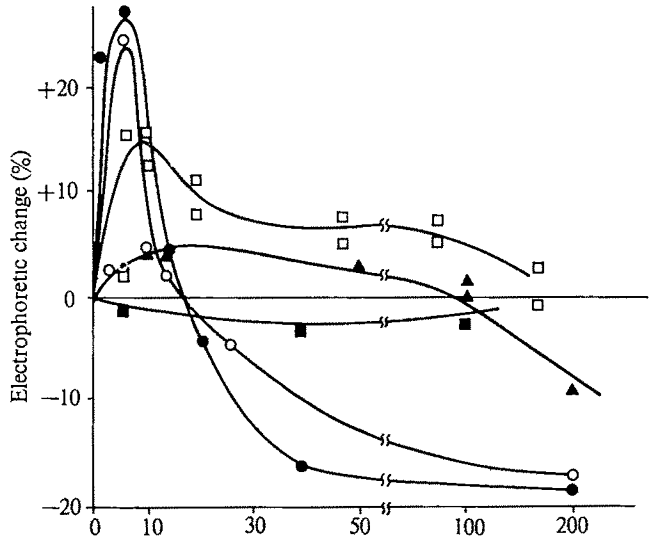


Fig. 2 Changes in cell electrophoretic mobilities induced by con A after treatment with enzymes Neuraminidase treatment 10^7 cells in 2 ml of incubation medium containing 0 02 M acetate buffered saline, *p*H 5 6, and 0 1 mM calcium chloride, were incubated with 10 units of neuraminidase (*Vibrio cholerae*, Calbiochem) at 37° C for 30 min Trypsin treatment 10^7 cells in 2 ml of incubation medium containing 0 1 M phosphate buffered saline, *p*H 7 0, were incubated with 20 μg of trypsin (Difco Co) at 37° C for 30 min Cells treated with enzymes were washed once with saline, and then incubated with con A as standard condition of contact ●, AH 66F pretreated with neuraminidase, ○, AH 62F pretreated with neuraminidase, ■, regenerating liver cells pretreated with neuraminidase, ▲, AH 66F pretreated with trypsin, □, regenerating liver cells pretreated with trypsin

washing once with 50 mM α-methyl-D-glucopyranoside or 100 mM D-mannose

Biphasic changes in the mobility of both strains of ascites hepatocarcinoma cells were amplified by treatment with neuraminidase When, however, regenerating liver cells were treated with 0 001% trypsin, biphasic changes in mobility similar to those occurring in the ascites hepatocarcinoma cells were induced by con A The increase in mobility of rat ascites hepatocarcinoma cells induced by con A was slightly inhibited by treatment with trypsin These results agree with previous reports describing cell agglutination after trypsinization[3,8] (Fig 2)

As shown in Fig 3, ascites hepatocarcinoma cells with markedly increased electrophoretic mobilities at low concentrations of con A (20–40 μg ml^{-1}) were more susceptible to neuraminidase than were untreated control cells There was also a noticeable cleavage of sialic acid from cells treated with low concentrations of con A Heat-inactivated neuraminidase had no effect

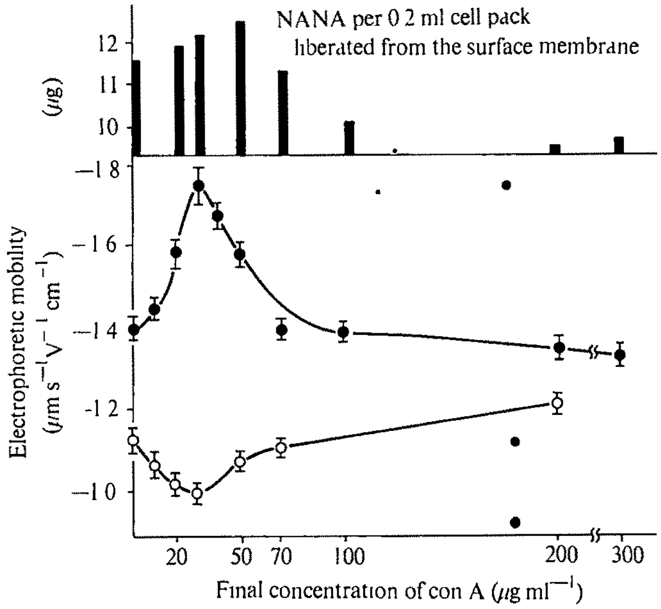


Fig 3 Effects of neuraminidase on AH 66F cells treated with con A Packed cells (0 2 ml) suspended in 2 ml of 0 02 M acetate buffered saline (*p*H 5 6) were preincubated with various concentrations of con A Ten units of neuraminidase were then added to each cell suspension, which was further incubated at 37° C for 30 min Just after incubation each sample was centrifuged The amount of sialic acid in each supernatant obtained was measured by the colorimetric method of Warren[15] A portion of remaining cells, after washing twice by centrifugation with 30 mM α-methyl-D-glucopyranoside and once with physiological saline, was used for the determination of electrophoretic mobility (○) A control experiment was also done with heat-inactivated neuraminidase and without washing treatments (●)

Although Vassar and Culling[16] and Currie[17] independently reported a decrease in the electrophoretic mobility of lymphocytes treated with some phytohaemagglutinins, at rather higher concentrations than those used in the experiment described here, they failed to find concentration-dependent biphasic changes in mobility We, on the other hand, have found that phytohaemagglutinin (PHA-P, Difco Co), induces biphasic changes in mobility of AH 66F and Ehrlich ascites carcinoma cells

Although there may be other explanations, we see the mechanism of the biphasic changes induced by con A as follows When low concentrations of con A bind to specific sites on the cell surface, the distribution of glycoproteins (and/or glycolipids) is changed Some of the sialic acid molecules attaching to the terminal position of saccharide chains and originally situated at deeper sites may shift reactively into the electrokinetic plane of shear of the surface membrane[18], so resulting in an increase in mobility. On the other hand, and in spite of the changes described above, when cells are coated with excess con A, bound con A molecules (Ip 7.1)[19] may cover negative elementary charges of cell surface. They are therefore too far below the new electrokinetic surface, resulting in a decrease in mobility.

We believe the data presented here are concrete evidence of changes in the surface membrane induced by con A, and that increases in mobility which we observed relate to conformational changes in the distribution of electrical charges in the surface membrane. Further investigations are needed to elucidate the correlation between agglutination and changes in the electrophoretic mobility of cells.

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Induction of Mitotic Synchrony by Intermittent Hyperthermia in Ehrlich Carcinoma *in vivo*

THE radiosensitivity of cultured neoplastic cells is generally highest during the mitotic stage of the life cycle[1,2], their sensitivity to chemotherapeutic agents is dependent on cell age in the division cycle[3–7]. If a method were devised for tumour systems *in vivo* to prolong the time when cells remain in mitosis or to synchronize mitotic activity in a predictable manner, the cell killing efficacy of ionizing radiation might be improved. If the same method could produce increased synchronization in any other phase in which cells are most sensitive to chemotherapeutic agents, an increased efficacy of these drugs might also result[2]. Techniques used *in vitro* to obtain synchronous populations involve selective harvesting[8], the use of chemicals[8,9] and the use of temperature[10–12]. Most *in vivo* synchronization attempts involve the administration of drugs which disturb cell progression. The pharmacodynamics of such treatments tend to limit severely the degree of synchrony attained. Recently, 33–38% synchrony has been reported for intestinal crypt cells *in vivo*, following mitotic combination drug treatment with arabinosylcytosine and colcemid[13]. Martin and Schloerb[14] increased significantly the mitotic activity of Walker 256 carcinoma cells in rats by intermittently raising the body temperature. If this technique proved to be reliable and the response predictable, the clinical implications are obvious. Radiotherapy during the mitotic interval of a synchronized population could result in increased cell killing with a possible decrease in the total dose, dose per fraction or concomitant number of fractions in a standard radiotherapy regime. These advantages could lead to more effective local tumour control with an increased therapeutic ratio.

Intermittent hyperthermia might also prove useful as a pretreatment to chemotherapy. Several commonly used antimetabolites and metabolic inhibitors are phase specific with respect to the cell cycle, with maximum efficacy during the DNA synthesis (S) phase. They include arabinosylcytosine[3], hydroxyurea[4], 2-pyridine carboxaldehyde thiosemicarbazone[5], methotrexate[6], 6-mercaptopurine[6] and 5-fluorouracil[7]. We have evaluated and compared the effects of intermittent hyperthermia on mitotic activity in tumours grown in the solid and ascitic form. Male Balb/c mice 8–10 weeks old (Simonsen Labs, California) were either inoculated intraperitoneally with 0.3 ml ($\sim 2 \times 10^8$ cells) of ascites fluid from a stock mouse carrying a 6–7-d-old Ehrlich ascites tumour or were injected intramuscularly in the left thigh with 0.3 ml of a cell suspension of Ehrlich carcinoma cells.

The heating apparatus consisted of a fully enclosed wire mesh cage with four separate compartments adjustable to variable distances above five 250 W infrared heat lamps. The lamps were connected in parallel to an automatic timer, permitting variability of the length of the heating period and the interval between periods.

To obtain the desired increase in body temperature, we first established the appropriate distance between the lamps and the cage. Mice killed by cervical dislocation immediately after having been heated for varying times and heat intensities had readings taken with a thermister probe inserted through an abdominal puncture. A plateau was reached at 41° C soon after the onset of heating, and this did not change significantly after an hour of heating. Further, the animals tolerated this increased temperature without serious complications. In subsequent experiments thirty-two mice (eight per cage) were intermittently exposed at a chamber height of 15 cm for 96 h. Mice with 2-d-old Ehrlich carcinoma in the ascitic form were subjected to either 14–25 min heating periods at 4 h intervals or 12–30 min heating periods at 8 h intervals. Untreated animals of the same age served as controls. Specimens of the ascites fluid were drawn from the live animals at 1 h intervals immediately following the last heat exposure (96 h after onset). One tumour specimen was obtained per animal. Smears were air dried, fixed in 10% buffered formalin or Carnoy's fixative, hydrated, stained for 11 min in aceto-orcein and counter stained for 30 s with 0.02% fast green[15].

Mice with Ehrlich carcinoma in the thigh with an average tumour diameter of 1.0 to 1.5 cm (approximately 2 weeks after transplantation) were heated for 15 min every 4 h for 96 h (twenty-four treatments in all). Mice were killed by cervical dislocation at 1 h intervals immediately following the last application of heat. The tumours were excised, fixed in Bouin's fixative for one day, dehydrated and embedded in paraffin. Sections, 5 μm thick, cut tangentially and centrally, were hydrated and stained as previously described with the exception that in the second 95% ethanol rinse, eight drops of concentrated NaH_4OH were used to remove the remainder of the fixative.

In a separate experiment eighteen untreated mice with 6-d-old Ehrlich ascites tumours were aspirated at 4 h intervals beginning at 0900 h to coincide with the time of collection for experimental tumours, accounting for the natural circadian rhythm of tumour cells in untreated animals.

All slides were examined under oil immersion, 1,000 times

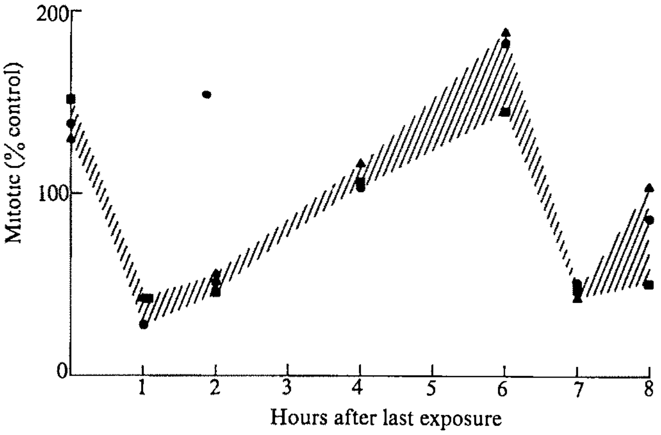

Fig 1 Relative effect of intermittent hyperthermia on the *in vivo* mitotic index of Ehrlich carcinoma in the solid and ascitic forms ●, Ehrlich carcinoma heated every 4 h, ▲ Ehrlich ascites heated every 4 h, ■, Ehrlich ascites heated every 8 h

magnification, with a Zeiss phase contrast microscope One thousand cells were counted in three separate groups per slide with three experimental slides per time interval after cessation of heat Cells in late prophase through late anaphase were included for estimating the mitotic index

Table 1 Mitotic Activity of Ehrlich Carcinoma grown in the Ascitic and Solid Forms in Balb/c Mice following Intermittent Hyperthermia

	Ascites 4 h*	Ascites 8 h†	Solid 4 h*	Controls
0‡	59 0§	68 0¶	62 0‖	39 7**
1	18 0	18 3	12 7	
2	24 3	20 3	22 7	
4	53 0	47 3	45 3	57 7
6	83 0	65 0	81 3	
7	18 7	20 7	23 3	36 7
8	46 3	23 3	38 7	

* 15 min every 4 h for 96 h
† 30 min every 8 h for 96 h
‡ Hours after last heating episode
§ $s\bar{x}=\pm 2\ 6$
¶ $s\bar{x}=\pm 2\ 1$
‖ $s\bar{x}=\pm 3\ 2$
** $s\bar{x}=\pm 4\ 7$

The mitotic indices (mitotic figures per 1,000 cells) found in the three experimental groups and controls are summarized in Table 1, and plotted as a relative function of time after the last exposure to control value (Fig 1) In the untreated mice mitotic indices of the tumour cells ranged from 39 7 at 0900 h to 57 7 at 1200 h and 37 7 at 1630 h These values were not significantly different from each other, and the overall average for untreated controls was 44 3 ± 4 7 In the three experimental groups the mitotic indices were significantly higher than control values at 0 h after the last heat exposure, with values ranging from 59 0 to 68 0

At 1 h, the mitotic indices in the experimental group varied from 12 7 to 18 3, significantly below the control values The mitotic indices then increased in all three groups to a maximum at 6 h with values ranging from 65 0 to 83 0 Seven hours after cessation of heat the mitotic indices decreased significantly to values of 18 7 to 23 3 and comparable to the 1 h values In the present experiments with Ehrlich ascites there was no indication as judged by body weight comparisons of heated and unheated animals that intermittent hyperthermia overtly modified the development of Ehrlich ascites

The use of high and low temperatures in obtaining mitotic synchronous cell populations has been used for *in vitro* cell systems as well as unicellular organisms such as protozoa[16–19] The present experiment and those by Martin and Schloerb[14] indicate that the maximum synchrony observed occurs 6 h after the last application of whole-body heat The present study extends these findings to a different tumour system grown in the ascitic and solid form The maximum values attained approach more than 180% of control values This induced synchrony seems to be independent of the heating interval as the results for the 4 and 8 h experiments with Ehrlich ascites cells were essentially the same It should be noted, however, that in the 8 h group, 6 h after the last heating episode, the increase was 143% that of controls compared with the 4 h group with 187% of controls Past *in vitro* studies show that hypothermia severely disrupts normal cell cycle progression[10,17,18] Similar results are obtained with *in vitro* and *in vivo* systems exposed to prolonged hyperthermia With chronic hyperthermia there seems to be a block of progression from metaphase to anaphase[17], a change in oxygen uptake[19] and periods of synchrony before reproductive death[10] The actual mechanism(s) involved in inducing partial synchrony with intermittent hyperthermia has not yet been elucidated The mechanism(s), however, does appear selective for neoplastic tissues[14,19]

Studies are in progress using tritiated thymidine pulse-labelling to determine if partial synchrony occurs in the DNA-synthesis phase Intermittent hyperthermia might shift the tumour cell population into more sensitive phases of the division cycle, enough to increase the anti-neoplastic action of ionizing radiation and chemotherapeutic agents

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Differential Effect of Myleran on Two Normal Haemopoietic Progenitor Cell Populations

MANY of the differential effects of cytotoxic agents used in cancer chemotherapy have been attributed to differences between the proliferation rate of normal and tumour cells[1,2] When certain closely related tumour cell lines are compared, however, the differences in sensitivity to cytotoxic agents cannot always be accounted for by differences in proliferation rate and the degree of proliferation dependence of some cytotoxic agents, observed with normal (non-tumour) cells, is frequently insufficient to explain the large difference in sensitivity between normal and tumour cells[3,4] It must be presumed, therefore, that there are inherent differences in sensitivity between tumour cell lines and also between tumour cells and normal cells

The method most widely used for determining the extent to which cytotoxic agents are proliferation dependent *in vivo* is to measure their effect on slowly proliferating stem cells of bone marrow in normal mice and in mice where these cells have been induced to proliferate more rapidly either by prior irradiation[4], by irradiation with marrow transplantation[5] or by treatment with endotoxin[6] The use of a single population of cells to test cytotoxic agents is important because it excludes inherent differences in sensitivity unrelated to cell proliferation rate We have found that two closely related cell populations of normal haemopoietic tissue have different sensitivities to the di-functional alkylating agent Myleran and that these do not depend on differences in the proliferation rate

The effect of Myleran (dissolved in dimethylsulphoxide and injected intraperitoneally as an emulsion with arachis oil) on the survival of bone marrow cells, which produce colonies in the spleen following transplantation into heavily irradiated mice[7], and on the survival of cells which produce colonies when cultured *in vitro* in agar, in the presence of a suitable colony forming stimulating factor[8], is shown in Fig 1 The response for each assay was measured 24 h after a single injection

The survival of agar colony forming cells is considerably greater than the survival of spleen colony forming cells This is not due to any difference in proliferation rate between the two cell types as the survival curve for each type of cell is unaltered for mice that have received irradiation previously (continuous γ-irradiation at 40 r d^{-1} for 2 weeks) to increase the rate of proliferation of both cell populations (R E M, N M B, and S F Okell, unpublished)

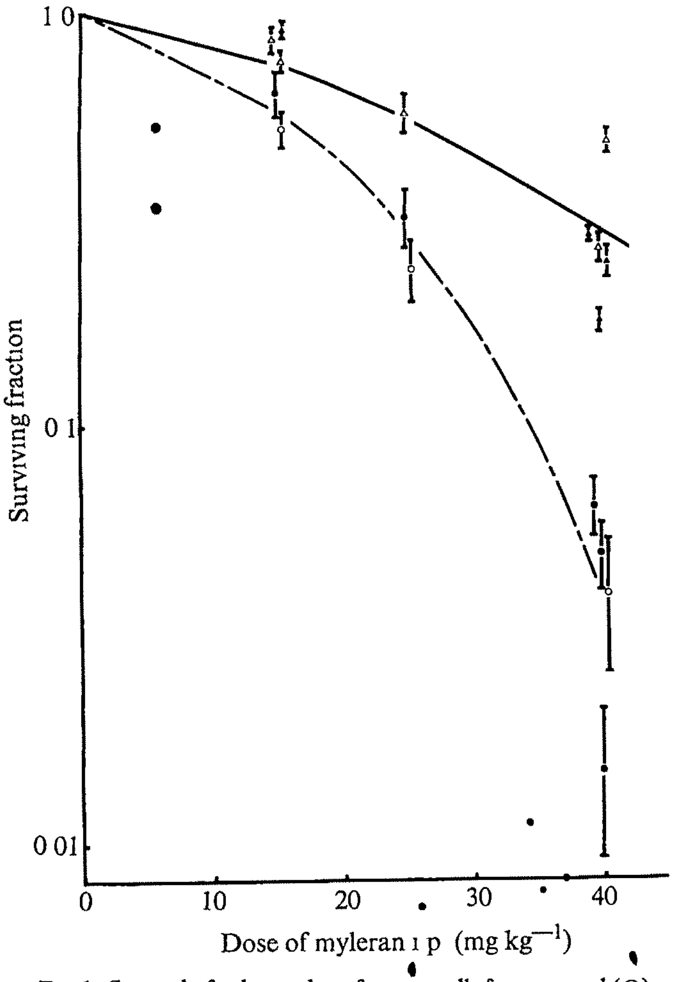

Fig. 1 Survival of spleen colony forming cells from normal (○) or irradiated (●) mice and agar forming colony cells from normal (△) or irradiated (▲) mice after different doses of Myleran

These results show that, as with tumour cell lines, closely related normal cell populations can also have appreciably different sensitivities to at least one cytotoxic agent and that these are not due to differences in the rate of cell proliferation This finding may have some relevance to cancer chemotherapy It is generally considered that the spleen colony forming cells, but not the agar colony forming cells, are the true multipotential stem cells of blood forming tissues As only the agar colony assay can be employed with human marrow, it is necessary to ascertain in what circumstances the two assays may be expected to be the same or to differ if this assay is to be used as an indicator of the response of the spleen colony forming cells

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Effect of *Toxoplasma gondii* on the Thymus

It has been shown[1,2] that rabbits experimentally infected with a virulent strain of *Toxoplasma* develop a severe lymphocytopaenia 3 d after infection and show marked changes in the thymus, chiefly by loss of cortical lymphocytes In a study of congenital toxoplasmosis in mice, Beverley and Henry (ref 3 and personal communication) observed depletion of cortical thymus lymphocytes beginning at the age of 5 to 7 weeks and increasing up to 8 to 9 weeks In mice infected at the age of 8 weeks thymic depletion was pronounced 16 to 30 d after infection but by day 51 the organ was almost completely restored In the present study we have paid particular attention to the effect of *Toxoplasma* infection in mice during the neonatal period

CBA and C57Bl mice were infected with *Toxoplasma* of low virulence (strain T626/62) within 24 h of birth The infectious dose was calculated to contain three to five cysts During an observation period of 6 weeks, about 25% of the infected animals died, some within the first week but most in the third week, when the infection seems to enter a critical phase

Groups of five to ten mice were killed at weekly intervals Total body weight and thymus weight were determined and material collected for histopathology, blood cell counts, serology and isolation experiments

In comparison with matched controls, growth was significantly retarded in infected animals (Fig 1) Thymus weights were also markedly reduced in relation to body weights

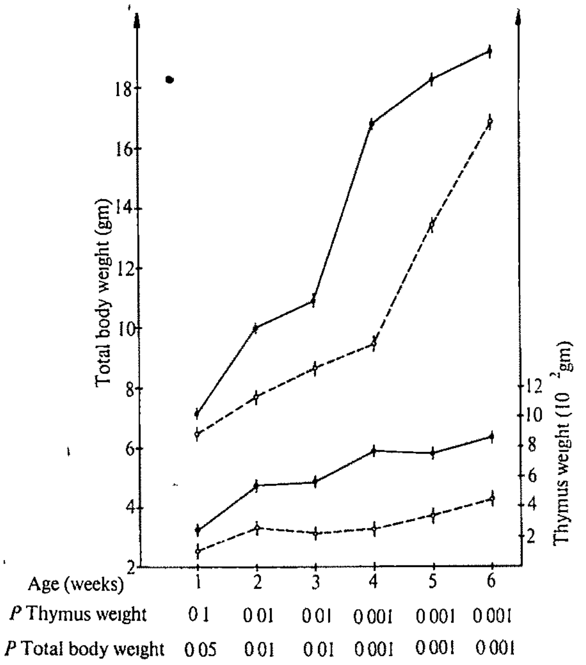

Fig. 1 Total body weight and weight of thymus in mice neonatally infected with low virulence *Toxoplasma* and in normal controls, expressed as means and s e for groups of 5–10 mice ——, Normal, - - -, *Toxoplasma* infected

Toxoplasma multiplication was moderate Only scattered foci, mostly consisting of a single infected cell, were demonstrable by immunofluorescence Before the age of 3 weeks such foci could be found in at least one of the organs examined (lymphoid organs, liver, lung, brain), but later only sporadically Toxoplasms were sometimes also found in the medulla or, less often, in the cortex of the thymus The infected cells were either macrophages or cells of the epithelial reticulum, with the methods used these two types of cell could not be distinguished Parasites were never found in thymic lymphocytes in sections or imprints Parasitaemia in low titres was demonstrable in almost all animals during the first 3 weeks and in several mice over the whole observation period

Depletion of cortical thymocytes was observed as early as the age of 1 week In pronounced cases, the thymus-dependent zones in lymph nodes and the spleen were also affected After 4 weeks, foci of large lymphocytes appeared subcapsularly in the thymus and a moderately increased activity of germinal centres in the spleen was observed, possibly indicating regeneration At no stage was lymphocytopaenia recorded Mice aged 4 and 5 weeks, however, showed increased counts of cells indistinguishable from small lymphocytes From week 2 a marked monocytosis appeared The amount of birefringent fat was markedly reduced in the adrenals[4] Dye test[5] antibodies were first demonstrable at 3 weeks In CBA mice high titres were recorded at 6 weeks, whereas in C57Bl the titres remained moderate

In a second series of experiments immunological reactivity to unrelated antigens was studied Neonatally infected animals were immunized at 3 or 6 weeks with one dose of either sheep red blood cells (SRBC) or inactivated poliovirus vaccine, and responses measured 4 and 12 d later by spleen cell plaque formation according to Jerne and Nordin[6] or 21 d later by neutralization tests according to Lagercrantz[7] Responses to both antigens were significantly reduced, as can be seen from Tables 1 and 2

In mice infected as adults, a marked effect on thymus weight and immune responses was observed At 3 weeks after infection a significant reduction in thymus weight was recorded In a group of animals infected at the age of 8 weeks and examined 3 months later, both size and histology of the thymus were normal When the response of these mice to SRBC was tested, however, they were significantly less reactive than age-matched controls (Table 3)

Table 1 Plaque Formation in Normal and Infected Groups of CBA and C57Bl Mice

Experiment No	Experimental animals	Direct PFC* per $10^5 \pm$ s e	t P	Indirect PFC* per $10^5 \pm$ s e	t P
1	CBA 3W N†	82±17	3 717	99±13	7 212
	CBA 3W TX‡	16±5	0 001	7±2	0 001
2	CBA 6W N	217±23	5 110	143±21	5 464
	CBA 6W TX	85±11	0 001	16±9	0 001
3	C57Bl 3W N	168±22	7 251	NT	
	C57Bl 3W TX	2±0 7	0,001	NT	
4	C57Bl 6W N	351±76	4 423	NT	
	C57Bl 6W TX	32±12	0 001	NT	

* PFC, plaque-forming spleen cells
† Normal mice
‡ *Toxoplasma* infected mice

Table 2 Neutralizing Antibodies to Killed Poliovaccine in Normal and Neonatally *Toxoplasma* Infected C57Bl Mice Antibody Level 10 d after Immunization

Experimental animal		Type 1	Type 2	Type 3
Normal	1	100	100	100
	2	400	400	400
	3	400	1,600	400
	4	100	100	100
	5	400	400	400
TX-infected	1	<100	<100	<100
	2	<100	<100	<100
	3	<100	100	<100
	4	<100	<100	<100
	5	≤100	100	≤100
	6	<100	100	<100

Antibody level 10 d after immunization

Table 3 Number of Plaque-forming Cells after 5 Months in Normal Mice and Those Infected with Low Virulence Toxoplasma

Experimental animals	Direct PFC per $10^6 \pm$ s e	t P	Indirect PFC per $10^6 \pm$ s e	t P
C57Bl N	204±37	5 032	253±47	5 042
C57Bl TX	15±2	0 001	18±3	0 001

Experiments were also designed to elucidate to what extent stress-mediated corticosteroid activity might be responsible for the thymolytic effect Mice were adrenalectomized at 5 weeks of age, and 5 d later they were inoculated together with normal controls with either virulent *Toxoplasma* (strain RH) or saline Animals were killed 24, 48 and 72 h after infection and total body weight, thymus and spleen weights, and blood lymphocyte counts were recorded The four groups did not show any differences in total body weight

A progressive loss in thymus weight was observed in infected animals, whether adrenalectomized or not (Fig 2) A few of the controls, receiving saline only, had slightly smaller thymuses than normal Spleens were significantly enlarged in all infected animals, equally so in both groups

Marked peripheral lymphocytopaenia was found in all unoperated, infected mice after 48 and 72 h, but in only 3 of 15 adrenalectomized animals

These experiments show that *Toxoplasma* infection affects both the anatomy and function of the thymus The mechanism of the effect is obscure, however, although it seems that adrenal activity might be a contributing factor The observation that adrenalectomy does not eliminate the effect indicates, however,

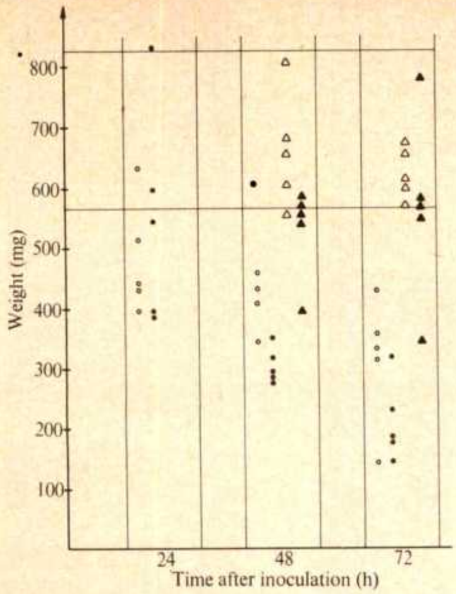

Fig. 2 Weight of thymus in 6-week-old CBA mice, untreated and adrenalectomized, given either 1×10^6 *Toxoplasma* of the virulent RH strain in 0.2 ml saline i.p. or injected with 0.2 ml saline only. Weights at three occasions, 24, 48 and 72 h after infection. Area within horizontal lines represents 95% confidence limits for normal untreated 6-week-old CBA mice. ○, Adrenalectomized, RH infected; ●, normal, RH infected; △, adrenalectomized, saline injected; ▲, normal, saline injected.

that the main cause has to be looked for elsewhere. A direct thymocytolytic effect of the toxoplasms can probably be ruled out, as they were never found in thymic lymphocytes, and experiments on cultured lymphocytes have failed to indicate any direct or indirect lytic effect of the parasite. The possibility of some kind of interference with the differentiation and migration of thymocytes should be considered.

Whatever the mechanisms, the long-lasting depression of immunological reactivity, which follows infection and persists after anatomical restoration of the thymus, might presumably have serious consequences in many situations. Recent publications show that *Toxoplasma* is not unique in this respect. Immunosuppressive effects of malaria[8], trypanosomes[9], and *Trichinella*[10] have been reported. It is likely that the widespread parasitic infestation in warm climates might render the population more vulnerable to other infections and account for the relatively poor responses to immunization that have sometimes been reported[11].

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Fatigue of Articular Cartilage

IT has been suggested[1] that fibrillation, the earliest change in osteoarthritic cartilage visible to the naked eye, may be the result of fatigue failure. Abnormally high stresses in the superficial layer of cartilage could be produced by unusually high applied loads, incongruity of the joint surface, or softening of the cartilage by mucopolysaccharide loss. Repeated cyclic loading could then lead to fatigue failure in the surface layer. To test this hypothesis postmortem human articular cartilage was subjected to repetitive compressive loads.

The apparatus was a vertically mounted electromagnetic solenoid, with a hemispherically-ended perspex indenter 3 mm in diameter attached rigidly to its core: weights were attached to the core above the solenoid. Specimens were mounted in a perspex bath containing Ringer's solution plus mycifradin sulphate (0.008 mg l^{-1}) and crystapan benzylpenicillin (0.05 mg l^{-1}). Two electronic timers provided repetitive switching of the supply to the solenoid and the frequency and duration of loading were set to 6 cycles $\min^{-1}$ and 1 s respectively. This allowed time for the cartilage to recover after each load application.

Fig. 1 An area on the superior surface of the femoral head after test, showing surface damage under the indenter.

Figure 1 shows an area of cartilage on the superior surface of the femoral head of a female, aged 47 yr, after 90×10^3 load cycles at a nominal stress of 2 MN m^{-2}. An Indian ink staining technique[2] was used before and after the test to indicate areas of surface damage. There was no evidence of surface fibrillation before the test. Figure 1 shows the circular area of surface damage under the indenter, as well as two broader markings; Fig. 2 shows that these broader markings have the same orientation as elongated splits produced by pin pricking. The surface damage is identical in overall appearance and orientation to the "minimal fibrillation" observed in osteoarthritic cartilage[2].

We obtained a measure of the mucopolysaccharide content of the cartilage by the fixed charge density method[3]. Before fatigue testing, full-depth specimens were removed

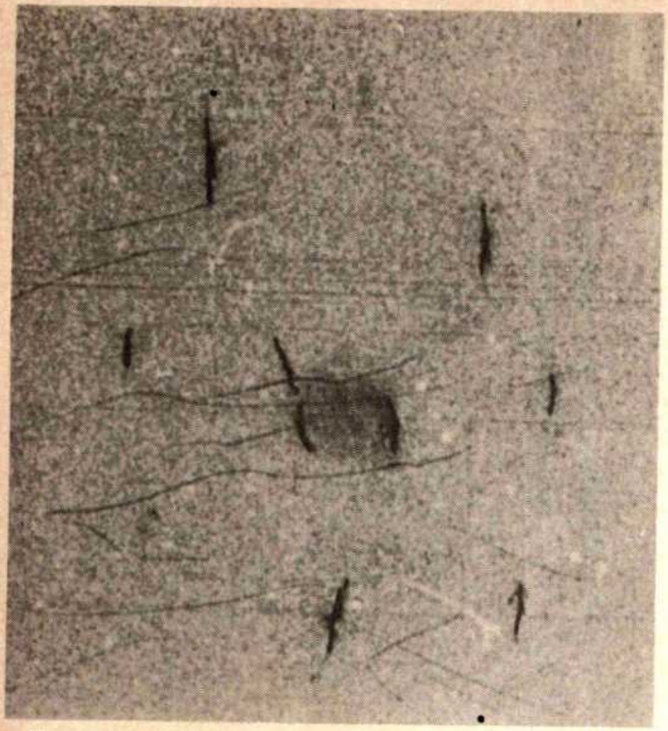

Fig. 2 Same as Fig. 1, but with damaged area surrounded by elongated splits produced by pin pricking.

with a cork borer 3 mm in diameter from two sites remote from the area to be tested and then were stored at −20° C during the test. After testing specimens were similarly removed from the tested area and three other areas. All six specimens were then cut into slices 200 μm thick. Plots of fixed charge density per wet weight of tissue against slice number below the articular surface are shown in Fig. 3. The similarity between the profiles of adjacent control areas taken before and after the test shows that there was no general loss of mucopolysaccharides from the femoral head during the test. A comparison of the profiles from the tested area and the adjacent control indicates no loss from the loaded area. All the profiles are typical of completely normal femoral head cartilage[4]. Clearly the surface damage produced during this test was not the result of a loss of mucopolysaccharide from the cartilage, either before the test or as a primary event leading to it.

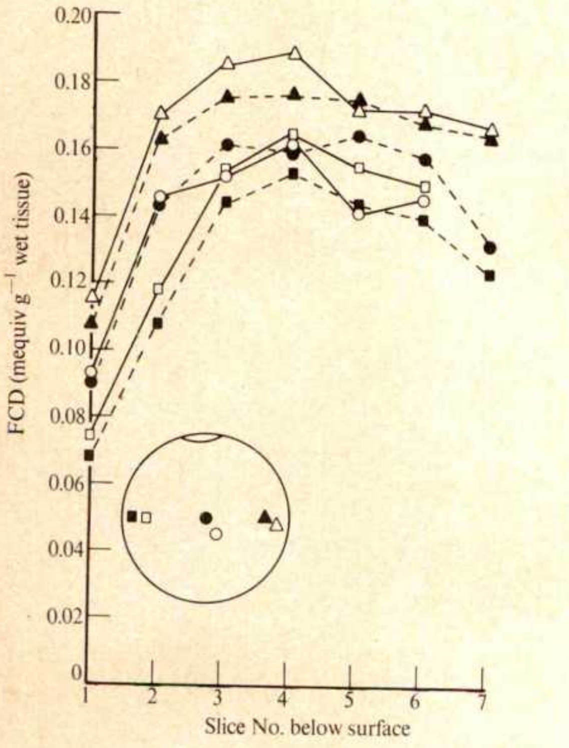

Fig. 3 Fixed charge density (FCD) calculated on a whole tissue basis, against slice number below the articular surface. ■, ▲, Before test controls; □, △, ○, after test controls; ●, fatigue area. Inset represents the sites of FCD specimens on the superior surface of the femoral head.

Although the results of only one test are reported here, other more preliminary experiments (without fixed charge density measurements) have been carried out and in identical condition all the tests produced similar surface damage. We conclude that surface damage of human articular cartilage, similar in nature to early osteoarthritic fibrillation, can be produced by a fatigue mechanism. Further work is in progress to study this phenomenon in greater detail.

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Monokaryotic Fruiting in the Basidiomycete *Polyporus ciliatus* and its Suppression by Incompatibility Factors

IN most of the higher Basidiomycetes production of fruit bodies is controlled not only by morphogenetic genes but also by incompatibility factors[1-3]. Generally, the morphogenetic genes can only express their information in matings between monokaryotic strains carrying different incompatibility factors. This leads by nuclear exchange to the establishment of a stable dikaryon and subsequently to the formation of fruiting bodies. In some rare cases, it has been observed that monokaryotic fruiting may be induced either by environmental[4-6] or genetic factors, that is, mutation of the incompatibility factors[7] or of other genes[6,8]. No definite hypotheses, however, concerning the cooperation of these genetic traits in controlling fruiting body production have been proposed.

We have obtained a stable dikaryotic stock of the wood destroying Basidiomycete, *Polyporus ciliatus* Fr. f. lepidus (Fr.) Kreisel, which forms fruiting bodies containing numerous four-spored basidia, when grown on corn meal agar, containing 3% malt extract, after 20 d at 25° C (Fig. 1). Oidia or other cells of vegetative propagation are not produced. Using the method described for Ascomycetes[9] we have isolated 100 basidiospores; from these, 85 spores germinated. Surprisingly, all of the resulting mycelia developed various kinds of stomatic structures which were more or less similar to normal fruiting bodies (Fig. 1). Approximately 70% of these abnormal fruiting bodies had hymenia. The basidia carried predominantly only two spores.

Cytological observations have revealed that these spores contained only one nucleus and the mycelia do not form clamp connexions. An inoculation of basidiospores from all monokaryotic fruitings unequivocally gave rise to the same phenotype. We conclude that these abnormal fruiters are true monokaryotic mycelia.

Testing these monokaryons in all possible combinations, we found, as expected[3], four mating types (A_1B_1, A_2B_2, A_1B_2, A_2B_1) which reacted according to the tetrapolar mechanism of the homogenic incompatibility system in the same way as known in other Basidiomycetes. This means that clamp connexions and normal fruiting bodies occurred only when A and B factors of both partners were non-identical. Common A or common B factors led to the typical "flat" or "barrage" reaction.

In the offspring of the compatible crosses we found the parental phenotypes and also new phenotypes which apparently arose by recombination. Complete genetic analysis of the monokaryotic fruiters, now in progress, should establish a variety of different genes, each of which are part of a sequence controlling the morphogenetic procedures leading to the differentiation of fruiting bodies. A similar sequence is already known for the Ascomycete *Sordaria*[10].

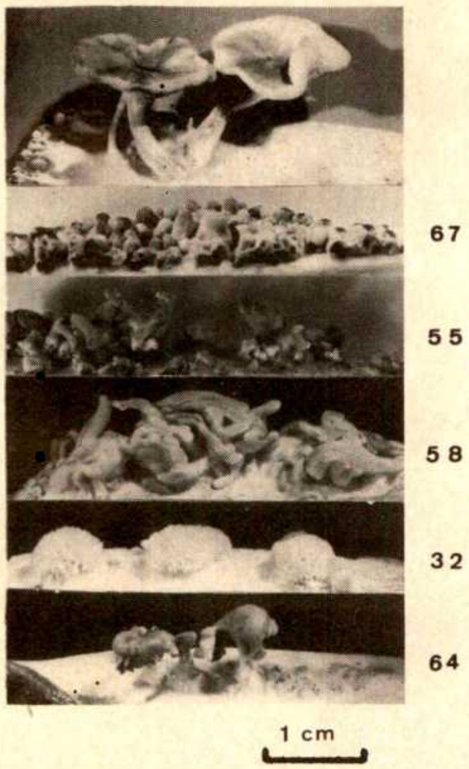

Fig. 1 Various types of fruiting bodies of *Polyporus ciliatus*. Normal fruiting bodies from the dikaryotic stock (top); abnormal fruiting bodies from monokaryotic strains, marked by their isolation numbers (below).

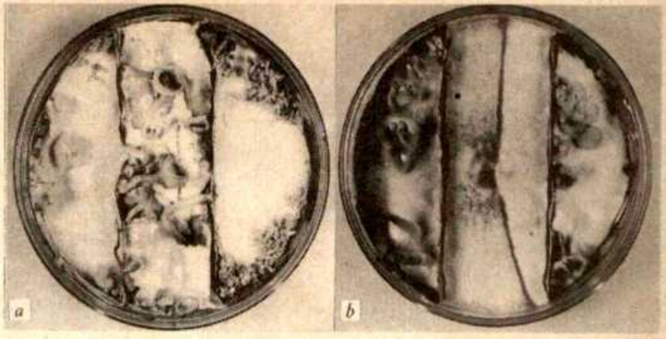

Fig. 2 Crosses of monokaryotic strains. *a*, Cross between strain 70 and 72 being compatible for both mating type factors. After inoculation of the dish the lateral parts of both partners have been dissected with sterile aluminium foil in order to avoid nuclear migration. Whereas the middle section has become dikaryotic and forms unequivocally normal fruiting bodies, both of the lateral sections show monokaryotic fruiting. *b*, Cross between strain 63 and 64 having common A and different B factors. Arrangement as in (*a*). As nuclear migration has taken place in the middle section, there is no fruiting body production, whereas in the lateral sections monokaryotic fruiting occurs.

During the crossing studies between the monokaryotic fruiters a new phenomenon was observed. In all crosses in which nuclear migration occurred (that is, unlike A and B, common A unlike B) the monokaryotic fruiting was inhibited as soon as the dikaryon or heterokaryon was established. Neither of the mating partners forms any kind of abnormal fruiting bodies in these regions which have become di or heterokaryotic (Fig. 2). As nuclear migration does not occur in common B combinations, no inhibition of monokaryotic fruiting was observed. The same holds true for combinations between like mating types which in spite of common A and B factors have become heterokaryotic. We conclude that the action of the genes responsible for the monokaryotic fruiting is suppressed as soon as nuclei with different incompatibility factors are in a common cytoplasm, regardless of whether normal fruiting bodies are formed (for example, $A_1B_1 \times A_2B_2$) or only sterile heterokaryons occur (for example, $A_1B_1 \times A_1B_2$). The original laboratory stock can therefore be considered to consist of a population of genetically different nuclei, each of which is unable to express its genotype unless the incompatibility factors present in the same cytoplasmic environment are identical and thus do not exhibit any suppressing activity. The regulating effect of the incompatibility factors is not only restricted to the first morphogenetic steps leading to the formation of a stable dikaryon with clamp connexions. The subsequent morphogenetic procedures which end with the formation of fruiting bodies are also controlled by these factors.

Our data, the details of which will be published elsewhere, are not only an example of cooperation between incompatibility factors and morphological genes, but will help to explain the phenomenon of morphogenetic differentiation. In addition, the suppression phenomenon may be used as a model to explain by a genetic mechanism the phenotypic balance of a population consisting of numerous genetically different nuclei.

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Shared Antigens of Parasitic Nematodes and Host Plants

ANTIGENS which metazoan parasites share with their warm blooded hosts have been known for many years. Examples of other "common antigens" can also be found among the viruses, protozoa, bacteria and their respective hosts. The occurrence and significance of this phenomenon has been the subject of a comprehensive review[1].

It has been demonstrated that immunological cross reactions occur between pathogens of plants and their hosts. Thus *Verticillium albo-atrum* possesses antigenic components found in cotton plants and antisera to *Ustilago maydis* cross react with antigens prepared from corn[2]. Some phytobacteria and their hosts also have antigens in common[3].

Wimalajeewa and DeVay[4] have shown that a common antigen relationship is a feature of compatible host-pathogen interactions. Host susceptibility may be dependent, therefore, upon successful molecular mimicry by the parasite. Other phenomena which may involve immunological cross reactions include species competition whereby the presence of one species is inimical to a second species[5] and the evolution of host specific strains in which morphologically identical organisms differ in host preference.

Plant parasitic nematodes and their hosts offer a unique model for the study of immunological cross reactions between host plants and metazoan pathogens. Nematodes such as the root-knot nematode, *Meloidogyne incognita,* live most of their lives in intimate association with host tissues, stimulating neoplasmic growth of the host and developing a nutritive relationship essential for the survival of the parasite. Successful establishment of a parasitic mode should therefore indicate convergent evolution of antigenic components. Molecular mimicry in plant parasitic nematodes would be remarkable, however, in that serologically similar proteins and other antigens are not known to occur in plant–animal relationships. To our knowledge, this communication is the first confirming their existence.

Eggs and larvae of *M. incognita* were collected from infected chili pepper, *Capsicum frutescens,* and pathogenicity of the larvae was tested on cotton, *Gossypium hirsutum*. For immunization of rabbits, surface sterilized eggs and freshly hatched, surface sterilized larvae were homogenized in a French pressure cell with 0.005 M phosphate buffer containing 0.001 M $MgCl_2$. Whole homogenates were used for immunization of rabbits and supernatants, following centrifugation (10,000*g* for 20 min) for immunodiffusion tests. Seeds of cotton and soybean, *Glycine max,* were germinated aseptically and, after 3 d of growth, the terminal 7–8 cm of root tip was excised and prepared[4] for immunization or use in immunodiffusion tests.

Antisera for plants and nematodes were produced in New Zealand white doe rabbits with a schedule consisting of intravenous, intraperitoneal and intramuscular injections over a 14 d period[4]. Antisera also were produced by three foot-pad injections given at 2 week intervals[6]. In homologous reactions, the agglutinin titres of antisera for eggs and larvae of the nematode were between 6,400 and 25,600 and for the host plants between 800 and 12,800.

Serological reactions were conducted in Ouchterlony[7] agar-gel diffusion plates. Antisera for eggs of *M. incognita* cross reacted with antigens from both hosts, cotton and soybean (Fig. 1) as did larval antisera. Antisera for cotton and soybean roots also cross reacted with antigens from larvae and eggs. In all cross reactions, at least one precipitin band was formed. In the case of cross reactions involving egg antisera and antigens from cotton, two precipitin bands were formed, only one of which was shared with soybean. These common antigens seemed to be serologically related to each other as the precipitin bands joined completely in agar gel diffusion tests. None of the antigenic preparations reacted with normal sera.

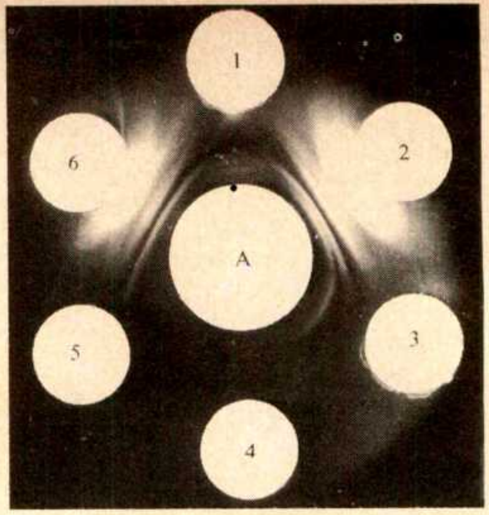

Fig. 1 Precipitin patterns in agar double-diffusion plates. The centre well (A) contained antiserum for eggs of *Meloidogyne incognita*. Wells 2 and 6 (1/2 dilution) contained homologous antigen and wells 1 and 3 antigens from cotton and soybean respectively. Well 4 contained buffer and well 5 1/4 dilution of cotton antigen.

Reports on the presence of an immune response in plants are not convincing[8–11]. While the presence of phytoprecipitin has been shown[12] the chemical composition and antigenic specificity of these substances have not been studied. The susceptibility of plants to infections cannot yet be explained in terms of immunological tolerance such as those suggested for animal-host systems. The occurrence of common antigens between plant parasitic nematodes and their hosts not only raises many interesting questions regarding the specificity of the host–parasite relationship, host resistance, nematode pathotypes, and so on, but reflects upon the origins of phyto-parasitism itself. Should common antigens represent structural or functional components, it would not seem surprising that parasitism in the higher nematodes (Tylenchida) seems to be almost as old as the origin of higher terrestrial plants[13]. If plant parasitic nematodes evolved from fungal feeding ones, further models for phylogenetic investigations using the common antigen approach are possible, because the latter are among the most abundant of the soil-dwelling Nematoda.

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Remote Sensing for Productivity in Pelagic Fisheries

IT has been argued that the reason for going into space is to obtain a better look at our own planet. One of the specific projects of NASA will be remote measurement of phytoplankton chlorophyll in the world's oceans, the practical use of this measurement most often mentioned relating to pelagic fisheries. A proponent is Dr Maurice Blackburn of Scripps Institution of Oceanography, who argues that the detection of phytoplankton concentrations by the measurement of chlorophyll may increase the efficiency of the tuna fisheries by reducing the scouting time necessary for the fishing fleet. Blackburn's arguments are based on a rather simple hypothesis that the distribution of a pelagic fish such as the tuna is controlled by water temperature and the availability of food[1]. His group has tested this hypothesis in an area off Baja, California, where large schools of tuna concentrate, feeding primarily on a red crustacean. The crustaceans in turn feed at least partially on the phytoplankton, which are abundant in this area. There is some feeling among fishery biologists that the Baja case may be an exception. Also, if the energy change through the food web is higher than the generally accepted value of 10%, small fluctuations in primary production observed in the open ocean may be too small to explain the yield of a particular fish or its distribution[2]. As Blackburn points out, tests with pelagic fishes are not easily arranged. The opportunity for testing the hypothesis in the Atlantic Ocean occurred when the research vessel Delaware made an exploratory fishing cruise across the North Atlantic Ocean, roughly between the Azores and the North American coast[3].

In addition to the longlining operation for tuna, standard hydrographical casts were made for temperature and salinity. Chlorophyll concentration was measured at six depths in the upper 100 m, following the method of Yentsch and Menzel[4]; total plankton volume was determined by hauling over 100 m a 0.5 m net (#6 mesh); volumes were determined using the method of Yentsch and Herbard[5]. The longline gear consisted of the Japanese type longline, with 160 fathom baskets with 87 hook design.

Largest tuna and total fish catches were made in the areas adjacent to the Azores in the North American continental shelf (Fig. 1). The big-eyed tuna dominated the catch in the eastern North Atlantic area and yellowfin in the waters of the mid-North Atlantic and Gulf Stream. Bluefin tuna were taken in the greatest numbers at the edge of the continental shelf south of Cape Cod. The big-eye tuna catch in the vicinity of the Azores reflected the catch of this fishery, which was in season at the time.

The volume of plankton and chlorophyll concentration (Fig. 1*b*, *d*) shows the same pattern of abundance as the fish (Fig. 1*a*, *c*). That is, plankton volumes and chlorophyll were highest near the eastern coast of the United States, lowest in the north central portion of the Sargasso Sea, and moderately high in the region of the Azores. The reason for the higher productivity near the eastern coast of the United States and the Azores is of interest because in both cases it is associated with ocean currents. Near the eastern coast of the United States, the dynamics of the Gulf Stream displace nutrient-rich water toward the surface and the same is true of the current moving toward the south in the region of the Azores. The magnitude of the latter is much less, and so the productivity is less.

The plankton and chlorophyll data support Blackburn's contention that in the open ocean, catches are usually greater in areas of high productivity, given that the fish are compatible with the water temperature. The data suggest that some type of aerial surveillance of chlorophyll

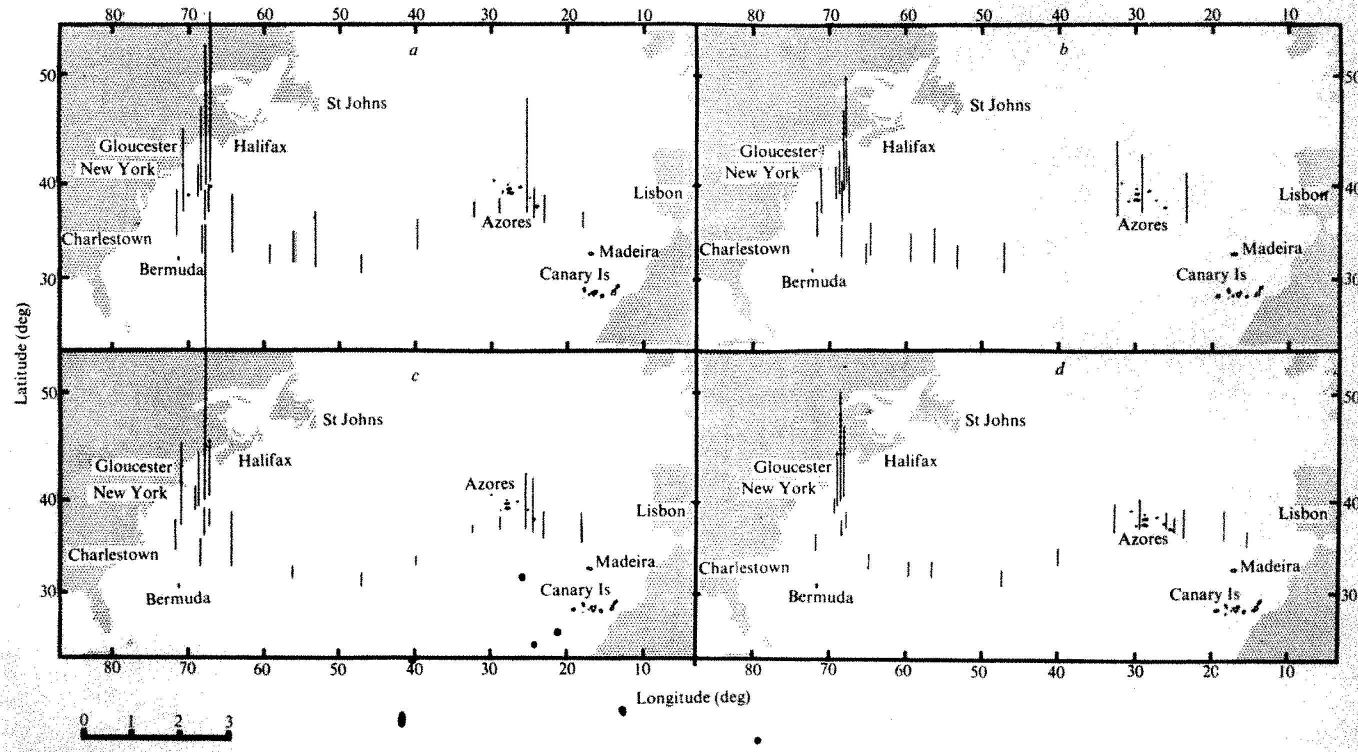

Fig. 1 Distribution of plankton and fish, April–June 1963. *a*, Total fish catch. One scale unit = 1.0 fish per hook per hour. *b*, Settled plankton volume. One scale unit = 10 ml. *c*, Tuna fish catch. One scale unit = 1.0 fish per hook per hour. *d*, Surface chlorophyll concentration. One scale unit = 0.60 μg l^{-1}.

from space would be useful. There are a number of difficulties in measuring chlorophyll from high altitudes, but recent experiments have shown that relatively simple measurements of ocean colour are an index of phytoplankton chlorophyll. It should be pointed out, however, that most of the differences of phytoplankton abundance throughout the world's oceans are the result of the same processes indicated here, that is, general oceanic circulation. Thus, global detection of water temperature alone could aid the pelagic fisheries.

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Possible Discontinuous Retinal Rod Outer Segment Formation in *Latimeria chalumnae*

THE outer segments of vertebrate rods are generally agreed to consist of stacks of closed membranous disks enclosed within the outer segment membrane, unlike those of cones which are continuous with that membrane[1]. In some cases the most vitread rod disks open to the ventricular space[2–7]. Work on the development of outer segments has suggested that the disks are formed by an infolding of the outer segment membrane in the region of the cilium[1].

Radioactive tracers have been used by Droz, Young and their colleagues to show that the proteins of rod outer segments in frogs, rats and monkeys are renewed from the vitread end. The label is first localized in the inner segment, migrates apparently through the cilium and forms a band at the vitread end of the outer segment. This band, which remains discrete, migrates sclerally, and is eventually lost from the rod tip, when it is phagocytosed by the pigment epithelium[7].

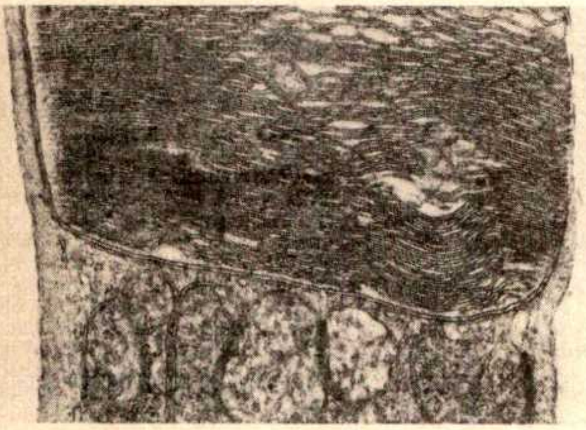

Fig. 1 Base of rod outer segment. The outer segment lamellae are enclosed within the plasma membrane, and are separated from the mitochondria of the inner segment by smooth parallel membranes. Because the cilium is not cut in this example the inner and outer segments appear to be completely separated.

The inner and outer segments are connected by a modified cilium, with a 9+0 pattern of double filaments; this is usually assumed to be the sole connexion, but Tokuyasu and Yamada[8], Pedler and Tilly[9] and Richardson[10] have demonstrated additional cytoplasmic continuity between inner and outer segments in mammals. Cohen[1] regards these examples as unusual and suggests that they may be intermittent phenomena.

During electron microscope studies on the retina of *Latimeria chalumnae* the bases of the rod outer segments have been observed to show two configurations. In about half of the rods the inner and outer segments appear clearly separated by a pair of parallel membranes. In examples where the cilium is not in the plane of section the membranes extend right across the rod (Fig. 1). Others, in which the cilium is cut, show the inner and outer segments in continuity only through that organelle, the parallel membranes separating them elsewhere.

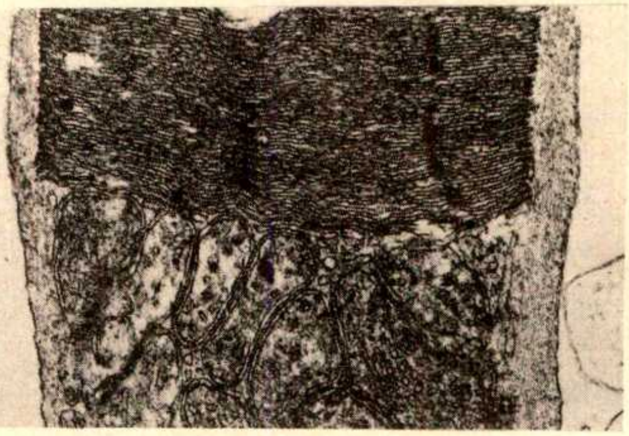

Fig. 2 In this example there is cytoplasmic continuity between the inner and outer segments, without the intervention of parallel membranes. Inner segment mitochondria are in close association with the basal outer segment lamellae, some of which are short and irregular.

Other rods do not show the paired membranes, and in these there is cytoplasmic continuity across their entire width. In these examples the inner segment mitochondria lie immediately adjacent to the outer segment base, and in places their surrounding membranes appear in series with those of the most basal lamellae. These basal lamellae usually include short ones which do not extend right across the rod (Fig. 2). In rods with this configuration and in which the cilium is cut, a lacuna is present between the shaft of the cilium and the inner segment cytoplasm. This lacuna probably represents a canal surrounding the cilium and open to the ventricular space, as described in mammals by Richardson.

These observations may be interpreted in two ways. It may be that all the rods have both an area of cytoplasmic continuity and one of separated membranes, and that the appearance of one or the other is due to accidents of the plane of section. If this is so some examples showing both features would be expected in a large sample, but none has been seen. The other possibility is that some rods showed one, and some the other, of the two configurations at the time of fixation.

If this were the case, the differences observed may not be permanent. The work of Young and his collaborators shows that outer segment protein is renewed from the vitread end as a continuous process, but that exfoliation of groups of disks from the rod tips is discontinuous. Our findings might be explained if the formation of disks is also discontinuous in *Latimeria*. The appearance in Fig. 2 would be consistent with a process of disk formation by, or in close association with, the inner segment mitochondria: that in Fig. 1 consistent with a period in which delimiting membranes had formed and the process of disk formation was in abeyance.

I thank the Royal Society for support during the International Expedition to the Comoro Islands in 1972, and for access to material collected during that expedition; the Danish Medical Research Council for support; and the Institute of Comparative Anatomy, University of Copenhagen, for hospitality during 1972–73.

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Haemodynamics in the Sauropoda

THE order Sauropoda includes the largest quadrupeds ever known. They were as long as 30 m and weighed as much as 80 t (*Brachiosaurus*[1]). To maintain an adequate blood supply to the brain in animals of such enormous size[2], physiological adaptation is essential. If pressures similar to those of mammals are required while the animal is erect then high aortic pressures are needed to overcome the hydrostatic pressure presented by the fluid column of the carotid arteries. Special stresses are imposed on the cardiovascular system of tall animals and rapid cardiovascular adjustments are required to compensate for pressure changes occurring, for example, during foraging.

The adult giraffe, standing from 5 to 6 m (ref. 3), has a vertical profile analogous to the large sauropods. Field measurements of carotid artery pressure, taken 40 cm below the jaw, revealed pressures of 125/75 mm Hg[4] in the quietly standing giraffe; recumbent pressures ranged up to 280/180. This study, and others[5,6], have substantiated that a range of pressures exists within an animal when the hydrostatic factor is relatively large. The hydrostatic factor which reduces arterial pressure in the brain increases it in the lower extremities when the body is upright.

To provide quantitative information on sauropod haemodynamics, I obtained the physical dimensions (Table 1) of two museum mounted specimens although how closely the mounted position of these specimens approximates a natural stance is difficult to assess. The position of the heart was estimated to be 46 cm below the second dorsal vertebra. Lateral measurements were taken to estimate the maximum levels to which the head could be raised.

Calculations based on the physical measurements (Table 2) ignore energy losses associated with tube dimensions and changes in blood viscosity. The values may be regarded as estimated minima if it is assumed that blood density approximated mammalian values of 1.055 g ml^{-1} and autoregulation of cerebral vasculature was present in sauropods. Maximum hydrostatic pressure would probably occur in *Apatosaurus* only when sitting or rising upright, but not while walking; forelegs were, however, longer than hindlegs in *Brachiosaurus* and maximum hydrostatic pressures while ambulatory would have been possible. The pressures derived from vertical distance measurements, calculated according to Burton[7], indicate proportional changes to increasing height in a resting fluid column.

Table 1 Physical Measurements of Two Sauropods

	Distance (cm)	
Vertical ↓	*Apatosaurus excelcus* Peabody, New Haven, Connecticut	*Brachiosaurus brancai* Humboldt, Berlin, Germany
1 Occipital condyle to ground	475	1,187 *
2 Second dorsal vertebra to ground	320	578
3 Last cervical vertebra to ground	305	590
Lateral		
1 Occipital condyle to second dorsal vertebra	518	980 *
2 Last cervical vertebra to occipital condyle	442	878 *

* Determined by triangulation with a Brunton pocket alidade by Dr John Ostrom.

These data predict mean systemic arterial pressures of 216 mm Hg (156+60) and 568 mm Hg (508+60) for *Apatosaurus* and *Brachiosaurus* respectively, in the mounted position. These estimates assume that a pre to postcapillary pressure drop of 60 mm Hg was sufficient to allow proper brain function and that the mounted position closely approximates a normal, upright stance. If maximum vertical heights are used the pressures are increased by more than 200 mm Hg in both genera. In dependent portions of the body, systemic pressure is increased by a heart to ground hydrostatic factor and pressures of 1,000 mm Hg could have been possible.

Table 2 Calculated Vertical Displacements and Hydrostatic Pressures in Two Sauropods

	Length (cm)		Hydrostatic pressure (mm Hg)	
	Mounted	Maximum	Mounted	Maximum
Apatosaurus				
Heart-brain	201	473	156	367
Heart-ground	274	—	213	—
Brachiosaurus				
Heart-brain	655	924	508	717
Heart-ground	532	—	413	—

Clearly the cardiovascular pressures in sauropods could have been enormous and this suggests that an appraisal of the assumptions used in estimating the pressures might be helpful. Is 60 mm Hg a realistic cerebral perfusion pressure? What evidence supports cerebral autoregulation or cardiovascular regulation in reptiles at any level? Figure 1 shows femoral arterial pressure in an anaesthetized iguana (*Iguana iguana*). This record was obtained at 28° C by cannulating the femoral artery with a saline-filled polyethylene catheter connected to a Statham 23A pressure transducer and recorded on a Grass model 7 polygraph. The record illustrates that systemic pressures approaching those of mammals are characteristic of at least some present-day reptiles. In addition, Hohnke (in preparation) has demonstrated that in the conscious iguana, arterial blood pressure is regulated during periods of haemorrhage and passive uptilting of the head. This indicates controlled pressure in the cerebral vasculature and provides evidence of cardiovascular compensation mechanisms in reptiles generally.

Accepting the high arterial blood pressures predicted by the calculations, it is interesting to speculate on structural

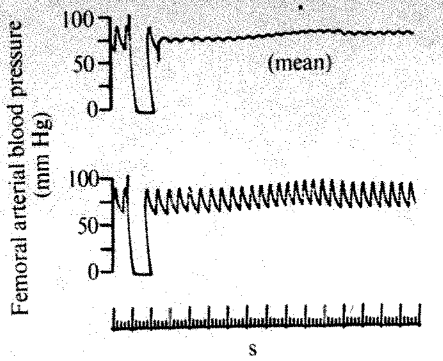

Fig. 1 Arterial blood pressure in *Iguana iguana*.

adaptations of the cardiovascular system. The law of Laplace has important implications for the structure of the ventricle when such high pressures are necessary. A small ventricular radius with thick myocardium would favour the maintenance of the required high cardiac pressures. Blood vessel structure was probably not too different from that of the giraffe. Arteries in the giraffe, such as the metatarsal, have large wall:lumen ratios[3]. Arteries closer to the head, carrying lower pressures, have lower ratios. Similar morphological changes accompany the development of essential hypertension in man[8].

Peripheral vascular beds such as muscle and kidney probably showed specialized adaptations also. In muscle, high capillary pressures could cause oedema unless counterbalanced by high plasma oncotic pressures. High filtration pressures in the kidney could enhance urine formation and require a considerable amount of energy for reabsorption of water and essential electrolytes. Precapillary attenuation of high arterial pressures would have been desirable and economical in both vascular beds.

The success of large reptiles during the Jurassic and Cretaceous periods proves that these animals solved the problem associated with great distances between the heart and the brain. Obviously, the exact cardiovascular values and specific adaptations of sauropods will never be known and inferences concerning their physiology must rest heavily upon assumptions. These calculations, based on skeletal measurements, have quantified in a limited way the haemodynamics of two sauropods and predict very high pressures in the aorta, and imply reflexogenic control over cerebral perfusion pressures.

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Competition and Diversity in Herbaceous Vegetation

GRIME[1] points out that herbaceous vegetation on highly favourable, "low-stress" sites often contains few species compared with that on intermediate-stress sites. He proposes an explanation for this which rests upon the claim that competition is less intense at intermediate-stress sites than at low-stress sites. I question this claim. The only evidence Grime gives to support it is based on a competitive index which he has devised. But he uses characters which are mainly related to competition for light, and seems to ignore the possibility of root competition. That root competition does occur between grassland plants is shown by experiments in which either shoot or root competition was prevented by partitions between the plants[2-7]. (Admittedly the conditions in such experiments are artificial.) Evidence that competition can be intense in species-rich grassland is as follows. (1) If seeds are sown into such vegetation and into control plots from which the vegetation has been removed, seedling establishment and growth are often better in the control plots[8,9]. (2) If some species are removed from established vegetation, some (at least) of the remaining species show increased growth[9,10]. (3) If organic nitrogenous fertilizer is added to the soil, the bulk of vegetation usually increases[11-14]. This shows that at such sites nitrogen is usually a factor limiting growth, and as nitrate and ammonium ions are mobile in soil, it is virtually certain that before addition of the fertilizer the plants were competing for nitrogen.

In my view, Grime's hypothesis should be altered, to state that when competition for light is intense, species diversity tends to be low; when competition for light is reduced, whether because of frequent cutting, trampling, low nutrient supply leading to intense root competition, or for other reasons, species diversity is often higher. I can suggest two possible reasons why competition for light, but not root competition, leads to low diversity. First, when plants are competing for light, a slight difference in tallness can give one plant a significant advantage, which with time "snowballs" until the shorter plant is totally suppressed[15]. In root competition it is doubtful whether any single character would confer such an advantage on one species. Second, when growth is limited mainly by light, there is little opportunity for small-scale habitat diversity, which would provide ecological niches. In contrast, in the soil there can be many niches; for example, plants can root at different depths, they can respond to small-scale variations in soil properties[16], and their roots can occupy different-sized soil pores[17].

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DR GRIME replies: There is a clear difference of opinion between Newman and myself with regard to the role of root competition in natural vegetation. It would be a mistake to pursue the discussion, however, without first defining competition and placing the phenomenon in a wider but relevant context.

Following the arguments (but not the wording) of Milne[1], competition between plants may be defined as the tendency of neighbouring plants to utilize the same quanta of light, ions of mineral nutrients, molecules of water or volume of space. This definition recognizes that competition is merely one component of Darwin's[2] struggle for existence and that in many habitats effects of competition are less important than those arising from differential susceptibility to the direct impact of the physiochemical environment or to damage by man and other predators. The need to observe these distinctions in the present discussion is obvious if we recognize that competition has led to the evolution of strategies which are different from those which enable plants to withstand extremes of environmental stress or predation.

I contend that the intensity of competition, above and below ground, reaches a maximum in fertile habitats where there is little damage by predators. The terminal role of shading in competition on fertile soils should not be allowed to obscure the fact that in such circumstances competition for nutrients is severe and may be of critical importance. An illustration of this is provided by the experiment of Donald[3] in which the superior competitive ability of *Lolium perenne* over *Phalaris tuberosa*, in conditions of high fertility, is pronounced only in treatments which permit root competition.

The weakness in Newman's argument is the assumption implicit in the phrase "low nutrient supply leading to intense root competition". Whilst it is clear that on nutrient deficient soils root competition is more important than competition for light, there are no grounds for supposing that the intensity exceeds that which occurs on fertile soils. From an examination of the relevant literature[4-8], I support the conclusion of Higgs and James[7] that there is no convincing evidence that plants indigenous to poor soils are more efficient in the uptake of essential nutrients. Moreover, field observations and experiments[9-11] strongly suggest that the ability of these inherently slow-growing[8] plants to survive in infertile habitats is related to their ability to persist for long periods in a state of chronic mineral nutrient deficiency and in this condition to resist the impact of climatic stress and the attentions of predators.

I would suggest, therefore, that the high species densities often encountered on unproductive soils are the result of the low competition in general rather than the shift in relative importance from shoot to root competition.

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Corrected Chromosome Number for *Spartina* in Ireland

ON the basis of the chromosome count of $2n = 126 \pm 2$ (ref. 1), *Spartina townsendii* H. & J. Groves was generally considered to be $2n = 126$ until 1963, when Marchant (ref. 2) first recorded $2n = 120$, 122 and 124 for plants in Britain. Seed-producing *S. townsendii* at Baldoyle near Dublin has also been found to have $2n = 124$ (ref. 3). A preliminary account of this grass was given in 1961 (ref. 4). The account is correct in general essence (ref. 3) but the chromosome number was incorrectly stated to be $2n = 126$ and a photograph used in illustration was misinterpreted as showing three quadrivalents and fifty-seven bivalents. In fact, the photograph shows one trivalent, one univalent and either two quadrivalents and fifty-six bivalents or sixty bivalents.

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Geological Antiquity of Rhodesian Man

CARLETON COON, in his book, *The Origin of Races*[1], argued that the "Caucasoid" (White) race, as represented by the well-known Swanscombe and Steinheim skulls, had crossed the threshold from *Homo erectus* to *Homo sapiens* in the Middle Pleistocene, at least by 250,000 yr ago, whereas the "Congoid" (Negro) race, as represented by the massive-browed and low-vaulted Broken Hill and Saldanha skulls, had remained at the *Homo erectus* level until well within the Upper Pleistocene, perhaps as recently as 30–40,000 yr ago. It has been pointed out that there are grounds for questioning the assignment of the Broken Hill and Saldanha specimens (lumped here and elsewhere as Rhodesian man) to *Homo erectus*[2] and few authors would agree that they can be assigned to any modern race, but most have accepted their Upper Pleistocene date. In this note I point out recent evidence that these specimens are in fact far older.

The principal Broken Hill specimen, nearly complete except for the mandible, was found by lead miners in a pocket of animal bones exposed in 1921 in a cave near Broken Hill, Northern Rhodesia (now Kabwe, Zambia)[3]. A minimum of twenty-three large mammal species were represented[4], including at least five extinct forms—a large baboon (?*Simopithecus*), a sabretooth cat (machairodont), a small warthog (?*Tapinochoerus*), a short-necked giraffid (cf. *Libytherium*), and a giant buffalo ("*Homoioceras*" = *Pelorovis*). A small and incomplete collection of artefacts that were probably associated with the skull was initially assigned by Clark[3,5] to the Proto-Stillbay industry (= Charaman of Cooke[6,7]) and more recently to the Sangoan[8], a terminal Early Stone Age ("First Intermediate") industry.

The more fragmentary Saldanha skull, which consists of a calvarium and a mandibular ramus fragment, was found in 1953 by Jolly and Singer on the surface at Elandsfontein (Hopefield), about 130 km north of Cape Town and 24 km east of Saldanha Bay, South Africa[9-11]. The faunal associations of the Saldanha skull are not entirely clear, because, like the skull, most of the faunal material has been collected from the surface, but it is probable that the hominid and the bulk of the mammalian taxa were roughly contemporaneous, as is suggested by Oakley's geochemical analyses of skull and animal bones[12]. Approximately fifty large mammal species have been identified[13], of which no less than nineteen are extinct, including most notably a giant baboon (*Simopithecus*), a sabretooth (*Megantereon*), a pig (*Mesochoerus*), a warthog (*Tapinochoerus*), a short-necked giraffid (*Libytherium*), a giant hippotragine antelope ("*Hippotragus*" *gigas*), a giant buffalo (*Pelorovis*), and various alcelaphine antelopes (especially *Megalotragus, Rabaticeras,* and *?Beatragus*). The artefactual associations of the hominid skull are difficult to establish, but it has generally been assumed that Saldanha man made at least some of the Acheulean (Early Stone Age) handaxes found at the site[14].

The radiocarbon dates that were available in the late 1950s and 1960s suggested that the Early Stone Age (s.l)/Middle Stone Age interface lay somewhere within the Upper Pleistocene, probably about 40,000 BP[8,15–17], and therefore most workers, including Coon, have assumed that the Broken Hill skull was roughly 40,000 yr old or even somewhat younger. The Saldanha skull has been considered older, but not necessarily very much so, because the handaxes with which it may have been associated were assigned to an "evolved" Acheulean (the terminal Early Stone Age or "First Intermediate" Fauresmith industry[14]). The archaic nature of the associated faunas, especially of the richer and better known assemblage from Elandsfontein, has been assumed to reflect the very late survival of quite archaic forms in sub-Saharan Africa.

Recent re-evaluation of the radiocarbon chronology of the southern African Stone Age by Vogel and Beaumont[18,19], based on an important series of fresh dates, clearly suggests that the Middle Stone Age may have ended, rather than begun, at 30–40,000 BP, and the Early Stone Age (s.l)/Middle Stone Age interface probably lies beyond the limits of the carbon-14 technique. Independent geological evidence for the unexpectedly great antiquity of the Middle Stone Age has been developed at the Klasies River Mouth and Nelson Bay caves on the southern Cape coast (South Africa), where long Middle Stone Age successions begin on and even in raised beaches probably dating from the Last (Eem) Interglacial[20–22]. By implication, the Early Stone Age (s.l)/Middle Stone Age interface may therefore lie in the Middle Pleistocene (that is, predate the Last Interglacial), and it is not even inconceivable that some so-called Middle Stone Age industries may date from well within that interval.

Recent analysis of the thousands of identifiable mammal bones excavated from the Middle Stone Age layers of the Klasies River Mouth caves suggests that the fauna, with a minimum of forty-three large mammal species, was essentially (generically) modern[22]. Only two extinct genera—*Pelorovis* and *Megalotragus*—were represented (the latter not certainly), and it is now known that both genera persisted until the very end of the Pleistocene (10–12,000 BP) in South Africa[23]. If the terminology of Cooke[24] and Wells[25] is followed and the essentially modern fauna of Klasies is assigned to the "Florisbad-Vlakkraal faunal span", then the implication is that the interface with the preceding "Vaal-Cornelia span" including the Elandsfontein and Broken Hill faunas must fall within the earliest Upper Pleistocene (Eem Interglacial) or Middle Pleistocene. Indeed an estimate of how old the Elandsfontein and Broken Hill faunas may be can be obtained from their broad similarity to that of Olduvai Upper Bed II through Bed IV[26,27]. Firm dates for these Olduvai units have not yet been published, but even the youngest (Bed IV) has been tentatively bracketed between 700,000 and 400–300,000 BP by a combination of palaeomagnetic evidence and extrapolated sedimentation rates[28].

In sum, the conventional Upper Pleistocene or even later Upper Pleistocene dating of the Saldanha and Broken Hill skulls, on which Coon partly based his argument, is almost certainly incorrect. The precise age(s) of the two skulls remains uncertain, but a combination of artefactual and faunal evidence suggests that they date from the later part of the Middle Pleistocene, more than 125,000 yr ago, if the best current estimate for the beginning of the Last Interglacial[29] is accepted as the end of the Middle Pleistocene. It is quite possible, perhaps even probable, that they are significantly older than the undoubted *Homo sapiens* skulls found in the Kibish Formation of southern Ethiopia and tentatively dated by Th/U to 130,000 BP[30,31]. Whether they are best regarded on morphological grounds as late *Homo erectus*[1,32] or archaic *Homo sapiens*[33–35], it is clear that they are much further back on the *Homo erectus–Homo sapiens* continuum than Coon thought, and certainly do not constitute good evidence for a very late persistence of *Homo erectus* in sub-Saharan Africa.

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Reconstruction of the Dental Arcades of *Ramapithecus wickeri*

SPECIES of *Ramapithecus* are among the few hominoid species currently considered as possibly close to the direct line of human ancestry. One of the most striking resemblances between *Ramapithecus* and later hominids is the supposed presence of parabolic dental arcades[1]. In view of the important evolutionary position postulated for these imperfectly known species we have made a reconstruction of the mandible and lower part of the face of the Kenyan species *R. wickeri* (Leakey)[2,3]. Previous attempts at reconstruction[4–6] have been necessarily conjectural because there were no midline points upon which tooth row divergence could be based. The mandible of *R. wickeri* (KNM-FT 45)[3] is so far the only specimen of this species, or of the closely related *R. punjabicus* (Pilgrim), that has the midline preserved at any point. It is also likely that it is associated with the maxilla specimen (KNM-FT 46).

A new examination of the left mandibular fragment shows that much of the symphysis is preserved. It now seems that the alveolus identified previously as that of the central incisor is actually that of the right lateral incisor and, further, that part of the medial wall of the right canine alveolus is also seen below it on the fractured surface. The anterior fracture across the symphysis is so low down that only the very deepest parts of the central incisor alveoli are seen on either side of the midline. The left lateral incisor root socket is preserved intact and was considerably larger than that of the central incisor; and the right lateral incisor socket is cut across longitudinally by the break in the mandible. The bony features of the symphysis are seen in the section in anterior view (Fig. 1) and a very low angulation is found to mark the midline on the anteroinferior symphyseal surface.

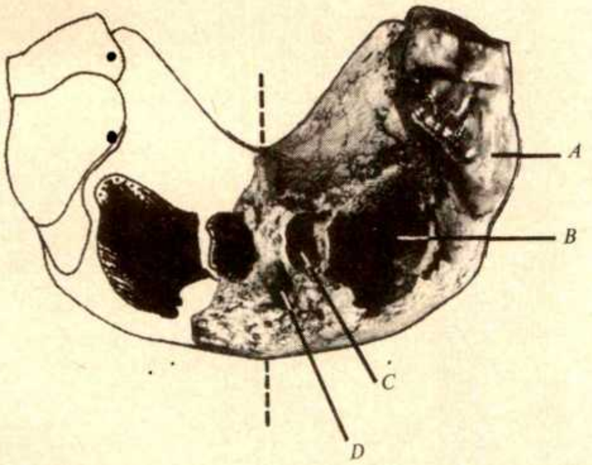

Fig. 1 Anterosuperior view of mandibular fragment, showing midline (dotted line). Missing parts of the right side are sketched in. *A*, P_3 crown; *B*, left canine alveolus; *C*, left lateral incisor alveolus; *D*, deepest part of left central incisor alveolus.

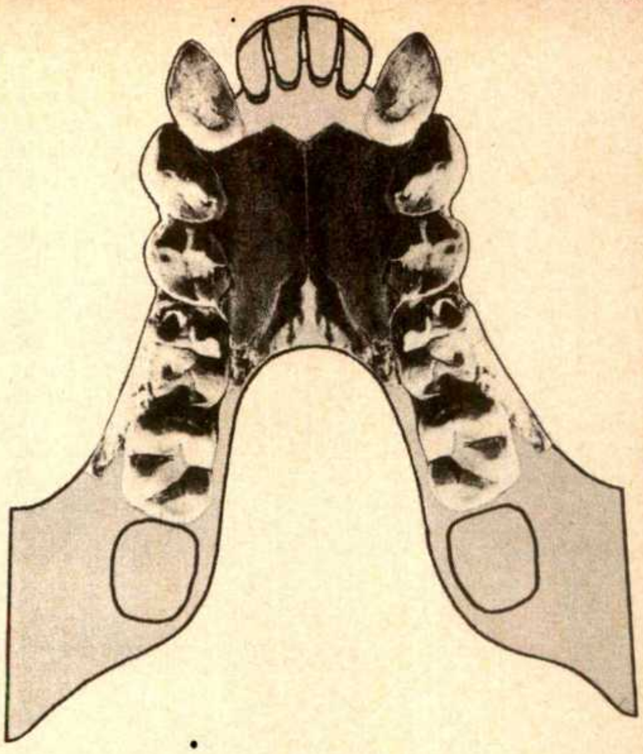

Fig. 2 Occlusal view of reconstructed mandible.

To make the reconstruction, mirror image replicas were modelled in plaster and joined to plaster casts of the original specimen. The mandibular antimeres could be accurately joined along the plane of the symphysis, as indicated by the dotted line in Fig. 1. To complete the reconstruction of the anterior part of the mandible the missing parts of the incisive alveolar margins were filled in following the contours of the surrounding good bone and an indication of the incisor crowns was modelled. The canines are based on a recently discovered right canine (KNM-FT 3318) and its mirror image. The posterior part of the reconstructed mandible is based partly on another undescribed specimen (KNM-FT 7), a right mandibular fragment with the crowns of P_4 and M_1 and the buccal margin of the body below P_4-M_2 preserved. Photographs and reversed photographs are presented rather than photographs of the model in order more clearly to show detail and the reconstructed areas.

The mandibular dental arcade is shown by the reconstruction to be very narrow anteriorly and the cheek-tooth rows to diverge posteriorly (Fig. 2). The anterolateral angle of the mandibular body is dominated by the jugum for the mesial root of P_3. In pongids the canine jugum marks the anterolateral angle of the body, but in *R. wickeri* the canine is mesiolingually placed with respect to P_3 and the long axes of these two teeth overlap each other over more than half their lengths. Similarly the incisors are mesiolingually emplaced with respect to the canine with the result that the anterior border of the mandible is abbreviated and the lingual border of the incisive alveolar margin is on a line that runs just mesial to the third premolars. The reconstruction emphasizes the great posterior development of the inferior mandibular torus which reaches as far as the level of M_1.

The left and right maxillary fragments (KNM-FT 46 and 47) were used for the maxillary reconstruction. These have parts not common to both sides and these parts were modelled on to the plaster casts of their opposites. This meant modelling, essentially, the canine and premolar region on the right fragment and the maxillary tuberosity and base of crown of the M^3 on the left fragment. The two completed parts were then placed in the best-fit centric occlusal position on the mandibular model and united in that position. The approximate size and shape of the M^3 crowns were judged from the crown outline present on the right maxillary fragment. The premaxillary region was modelled as a functional counterpart of the anterior end of the mandibular model. This reconstruction is shown in Figs 3 and 4.

As in the mandible, the maxillary tooth rows are shown by the reconstruction to be anteriorly approximated and to diverge posteriorly (Fig. 3). The palate appears relatively long and narrow and an estimated index (internal width between the first molars/C-M^3 tooth row length) is 40%. This compares well with values for the gorilla (35–50%), is lower than for the chimpanzee (54–71%) and is much lower than values for modern man. Alveolar prognathism is slight and the premaxillary region is quite abbreviated. As judged from the remaining portions of the zygomatic processes, the face was extremely flat and broad posterior to the canine fossa. A full face view of the

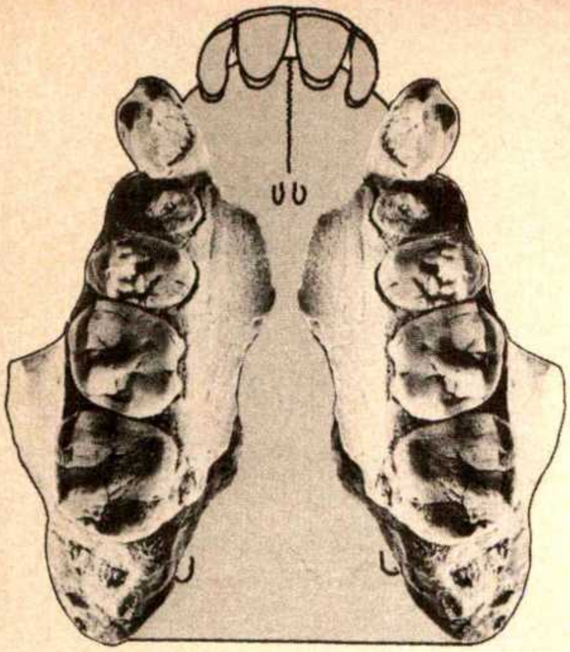

Fig. 3 Occlusal view of reconstructed palate.

reconstruction was attempted but is not presented because the shading of the missing portions obscures the photographs almost entirely.

The outlined shaded portions of the reconstruction in Fig. 4 are based on filling in between known points or on regressions based on known measurements. Regressions between variables were based on a sample of forty-eight modern primate skulls (eleven *H. sapiens*, twenty-five pongids and twelve cercopithecoids). A regression of nasopinale to alveolare on zygomatic height (cervical border of M^1 to highest point on the zygomatic process of the maxilla) gave a mean nasospinale-alveolare distance of 16.0 against a measured zygomatic height of 13.1. This estimated value is the same as that measured on the original *R. punjabicus* maxilla YPM 13799. Another facial estimate was obtained from the regression of the minimum distance from the floor of the orbit to the cervical border of P^4 on zygomatic height, which gave a mean value of 29.6.

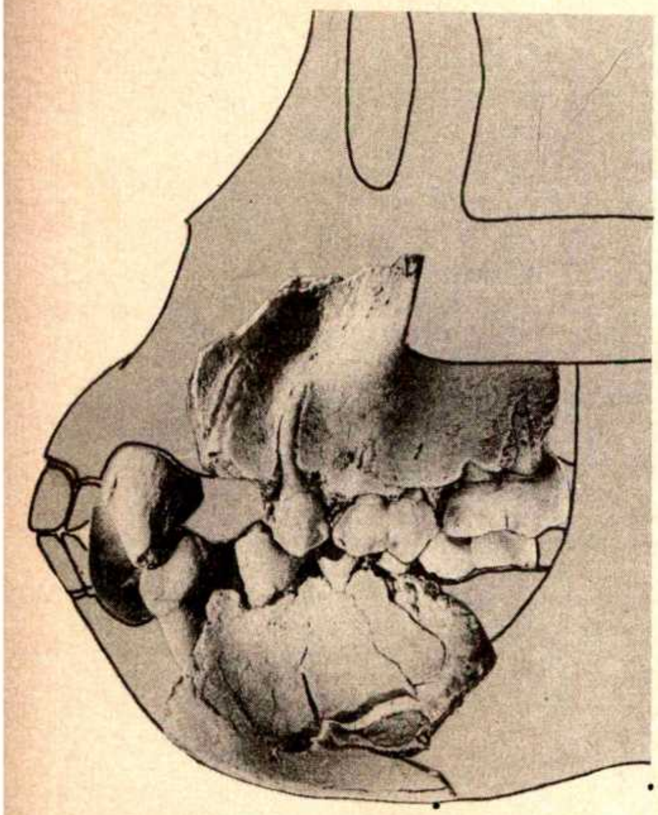

Fig. 4 Lateral view of reconstructed mandible and maxilla.

Several points arise from this reconstruction. It seems likely that *R. wickeri* had very small incisors indeed and posteriorly diverging and nearly straight cheek-tooth rows, rather than widely separated and curved tooth rows such as are found in modern man. The palate is narrow and the tooth rows are relatively very elongated. The premaxillary region was most likely abbreviated and a small snout with a small piriform aperture projected from a broad and very flat face that was especially wide in the zygomatic region. These peculiar and unique gnathic features very clearly place *Ramapithecus wickeri* apart from contemporary species of *Dryopithecus* and also make it clear that it did not have the rounded dental arcade postulated from previous reconstructions.

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Reasoning and Piaget

THE recently published article by Bryant and Trabasso[1] gives the impression that something significantly new about children's inference has been discovered which, in turn, challenges Piaget's[2] analysis of operative development. The thesis and the data on which it is based deserve critical commentary because the first claim is questionable and the latter is incorrect.

The authors assert that they were able to measure "genuine transitive inferences" in children as young as 4 yr because they eliminated memory as a factor whereas other investigators did not. Children were trained and overtrained to discriminate sequential pairs of rods AB, BC, CD, DE; the rods differed in colour and children had to label each rod with a name, big or small. The critical test was nonsequential pairings of the rods BD, success on which was said to be an inference based on memory for the old pairs: the probability that rod B is called longer than rod D is jointly determined by probabilities of recalling that B was bigger than C and that C was bigger than D.

With the exception of comparing the obtained with the expected success on new pairs, no experimental manipulation of the memory factor was made and neither frequency of pairings nor time was varied. The authors did not manipulate the pre-inference sequence, a condition which is known to implicate memory on this kind of problem[3] and their interpretation of memory is, therefore, far from convincing.

In the light of established literature on this problem, the absence of controls which might have made the data clearer is inexcusable To show inference, investigators have usually asked children to judge pairs of rods in conditions of varying amounts of information Control conditions included (1) showing BD without other prior comparisons, (2) showing BD after pairing each with other rods, but not with a middle term[4], (3) varying transity itself by having the same subjects judge BD after premises $B>C=D$, $B=C>D$, and $B>C>D$[3-5], (4) having BD judged in comparative conditions when logical and perceptual information would be in conflict[6], and (5) neutralizing possible designations of B and D in absolute size terms Bryant and Trabasso[1], who used only the last control and found no age differences, cannot claim that they discovered a reasoning capacity apart from memory unless they found subjects who successfully learnt the original paired discriminations and failed on the BD pairing Thus in their design, memory, learning, attention, and inference are inextricably confounded and cannot be related to a developmental framework

Apart from irregularities of method we question the naive assumption of the authors that any size discrimination not based on a direct perceptual encounter is *ipso facto* logical reasoning Usually in an inference, a necessary, logical conclusion is drawn from a set of premises But here we have no more than a perceptual consistency, children were working with arbitrary relations among differently coloured rods To be parsimonious, their subjects can be said to have performed consistently in judging new pairs in an organized system dictated by the old, overlearned pairs

This may be a type of inference arrived at by perceptual generalization or consistency but it is obviously different from logical inference studied by Piaget Other investigators[7,8] have also studied "sub-logical" inferences and found that very young children are capable of consistency in responding to new items through relations entailed by old Huttenlocher[9] has shown that persons can reason according to relations in an imaginational manner through which the common link is reinstated For example, when Charles is bigger than Mary, and Mary is bigger than Bill, the child imaginally orders Charles>Mary>Bill and concludes that Charles is bigger than Bill It has also been shown that children can order colours in this same way[7,8], the requirement in the task of Bryant and Trabasso[1]

More important than the methodological weaknesses and alternative explanations of the data is the criticism levelled at Piaget's theory A rereading of Piaget's work would show that the situations in which Piaget has studied transitive inference do not entail memory processes For example, the child stands between two towers of blocks, each on a table of differing height, and is asked to find out whether the two towers are the same or different in height Piaget observed that children below ages of 6 or 7 yr guessed, used visual estimation, or improvised imprecise measuring tools such as an arm span Older subjects used logical strategies for obtaining a certain answer They made use of material with which to measure the comparative heights so that the measuring instrument became a logical middle term for example, $A>B$, $B=C$, therefore $A>C$

It does not seem reasonable to claim that Piaget's observations of an age separation are explained by a memory factor Younger children did not use a measuring device, or when they did so its use was unreliable Older children used devices which allowed for sure judgments For all children the towers and potentially usable middle terms were always present on the tables in front of the children, consequently there was no information to remember or forget

In fact, Bryant and Trabasso's work is not germane to Piaget's observations, it refers to studies of other investigators who have used the method of successive discriminations But, as we said before, memory has already been found to play a role in this kind of study and with adequate controls Piaget's developmental model has been supported

Perhaps a broader issue is involved here Today, Piaget's theory seems fair game to almost any type of reductive analysis based on elementary processes like memory, attention, learning, and so on It is not clear where these several polemic arguments are leading us On the one hand, they attempt to discredit the theory even though Piaget has recognized the importance of these processes in operative development[10] On the other hand, they offer little in terms of constructive alternatives A broader perspective like that taken by ethologists[11] would be more helpful in the task of uncovering the relation of learning to development Fortunately for students of human development, Piaget's theory has already provided a foundation from which we can build

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DR BRYANT replies Youniss and Furth make three main criticisms of our article[1], all of which seem to me to be misguided The criticisms are that we did not manipulate the memory variable, that the inferences which we detected may have been "sub-logical" and dependent on imagery and that Piaget's techniques did not involve memory and therefore are not open to the criticism which we make of them I shall take these points in order.

We concluded that memory was the variable which led to failures in other experiments and not in ours, because no care was taken in these experiments to ensure that the children remembered the information which they had to combine inferentially, while considerable care was taken in ours This seemed to us the chief difference between our technique and those of others Of course, these were the first two experiments in a series and in subsequent work I did manipulate the memory variable By a trial by trial analysis of what the child remembered and of his ability to reach the correct inference, I was able to make a direct relation between memory and inferences I showed that as soon as children remembered the necessary information they could combine it inferentially This work is reported in a recent publication[2]

In our 1971 article[1], we showed that children could combine information in a logical transitive inference, which means that they could work out that $A>C$ from the information that $A>B$ and $B>C$ Whether this was done through imagery or by some other means of representation is another question which does not affect the logical status of the inference Indeed, it is rather ironical that Youniss and Furth quote Huttenlocher[3] at this point because she has done a great deal to show that adults often use spatial imagery to solve logical problems and that in doing so they are being perfectly logical There are no grounds for thinking, as Youniss and Furth suggest without any substantiation, that the use of spatial imagery in these problems is "sub-logical"

Their suggestion that Piaget's techniques did not involve memory is most surprising. Their "rereading" of Piaget's work has not been complete and they have missed a basic distinction made by Piaget himself between experiments of the type which we are criticizing and experiments involving "spontaneous" inferences.

Piaget has done experiments in which children were shown first that A>B or A=B, then that B>C or B=C and finally were asked to make an inference about A and C. He has given clear descriptions of such experiments in which the quantities involved were weight[4], volume[5] and size[6,7]. These are the experiments which we are criticizing, as they involve memory as well as inferences.

Youniss and Furth's suggestion that Piaget did not use this technique is, therefore, inaccurate. They wrongly state that his experiments are only of the "spontaneous" variety where the child not only has to make an inference, but also has to provide for himself the information on which the information must be based. We are not criticizing these "spontaneous" experiments and, indeed, I have suggested elsewhere[2] that the conclusions drawn from them are basically correct.

Finally, a comment on the statement that Piaget's theory "seems fair game to almost any type of reductive analysis based on elementary processes like memory, attention, learning etc." In our paper we were not trying to reduce the theory, we were simply trying to point out that the statement that young children cannot make transitive inferences was based on poorly designed experiments. Youniss and Furth have done nothing to show that the design of the traditional experiments on transitive inferences is any better than we suggest it is. They seem to be saying that the breadth of Piaget's theory excuses him from carrying out properly designed experiments. I cannot agree with this uncritical approach.

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GENERAL

Gamma Distribution in Consumer Purchasing

A LONGSTANDING assumption in the theory of repeat buying has now been explained by results on consumers' brand switching behaviour first published a few years ago[1] together with more recent findings concerning the independence of brand choice and weight of purchasing.

The NBD theory of repeat buying for frequently bought branded consumer goods rests on two assumptions: (i) Purchases of a particular brand by a given consumer in successive equal time-periods are independent and follow a Poisson distribution with constant mean. (ii) The mean rate of purchasing varies from consumer to consumer and follows a gamma distribution in the whole population. One consequence of this model is that the frequency distribution of purchases of a brand for the whole population in any given time period should follow the negative binomial distribution (hence the name of the NBD model). This and other deductions have generally been found to hold in thousands of cases over the past 15 years[2-4].

There has been considerable evidence supporting the Poisson assumption, and showing that the NBD model is not sensitive to such departures from the Poisson assumption as do occur[2,5]. There is also overwhelming empirical evidence that different consumers have different mean purchasing rates, but there has been no direct evidence for the assumption that these differences should follow a gamma distribution.

However, a direct explanation for the appearance of the gamma distribution is provided by applying a theorem of Mosimann[6] to the observed regularities in consumer brand-choice behaviour. This theorem, based on a powerful characterization of the gamma distribution due to Lukacs[7], is as follows: "Let Y_i ($i=1, 2, \ldots, g$) be g non-degenerate and positive random variables, and suppose that they are independently distributed. Let $W=\sum_{j=1}^{g} Y_j$ and define the random variables P_i ($i=1, 2, \ldots, g-1$) by $P_i = Y_i/W$. Then each of the $(g-1)$ random variables, P_i, is distributed independently of W if and only if all Y's have gamma distributions with the same scale parameter."

Applying this to consumer purchasing for a product-field with g brands, Y_i represents the average rate of buying brand i across different consumers, W represents a consumer's rate of buying the product-field as a whole, and P_i the proportion of a consumer's total purchases which is devoted to brand i.

Now the brand-switching results reported earlier[1] provide evidence that the purchasing rates Y_i are nearly independent, the correlations between them being generally very small. There also is now extensive empirical evidence that the P_i are approximately independent of W, for instance, the share of purchases devoted to each brand is generally much the same amongst light, medium and heavy buyers of the product-field[2].

These empirical results together with Mosimann's theorem explain why the variation across consumers of the rate of buying a brand should approximate a gamma distribution. It also provides a link between the theory of repeat-buying of a single item and that of brand choice between different items. The development of a comprehensive model of buyer behaviour embracing single-brand and multi-brand aspects is proceeding.

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Reference Abbreviations

FROM September 1 it is *Nature's* intention that all abbreviations of references should conform to the style of the *World List of Scientific Periodicals*, fourth ed. (Butterworth, 1963–65). The changeover will be gradual and authors submitting manuscripts from now on are asked to ensure that the references are written appropriately.

BOOK REVIEWS

Farming in British India

Agrarian Conditions in Northern India By Elizabeth Whitcombe Volume 1 *The United Provinces Under British Rule* 1860–1900 Pp. xxviii+330. (University of California Berkeley, Los Angeles and London, 1972) $12

AFTER the "Mutiny" uprising of 1857–1858 the Crown finally took over full responsibility for the government of British India from the East India Company and with almost missionary zeal embarked on an endeavour to bring the benefits of western civilization and scientific and technical innovation to the subcontinent India was clearly a potential source of great wealth for Britain but official policy would be to act on the model of the enlightened British landlord, conscious of his duties as well as his privileges Through public works, especially irrigation, the productivity of the land was to be increased many-fold, thus bringing security, greater prosperity and increasing revenue to the administration

Dr Whitcombe, in the first of her two-volume study of agrarian conditions in Northern India, describes the practical effects of this policy on the rural population of the North Western Provinces and Oudh (which together now comprise the state of Uttar Pradesh) in the 40 years after the "mutiny". That a book of this kind is at all possible is due to the existence of a mass of statistics and first-hand observation contained in numerous contemporary reports, most of which are now housed in the India Office Library and Records in London Dr Whitcombe has studied these with great thoroughness. Many of the settlement officers and other authors of technical reports were percipient and sensitive observers and were candid in their criticism of government policy The author frequently quotes them verbatim and to good effect in documenting her account

The book begins with a description of the existing pattern of rural life, the complex cropping sequences and intricate community structure, both of which had evolved to cope with the vagaries of the monsoon climate The author then goes on to describe the development and effects of the massive irrigation programme which was based on the construction of the Ganges, East Jumna and Agra canals The second half of the book is devoted to the revised tenancy laws which the administration introduced, the new "scientific" evaluation of land for the purposes of revenue collection and the effects of both of these on the pattern of rural indebtedness The final chapters describe the pressures and dilemmas which increasingly faced the courts and the whole administrative structure At times the wealth of detail in the book tends to overwhelm the reader The constant recourse to vernacular names in describing the elements of the agricultural system and the positions and functions within the social hierarchy demands frequent reference to the glossary But in the end this attention to detail wins through and reinforces the authority of Dr Whitcombe's case

The book presents a formidable indictment of British policy The canals, it is true, had greatly increased agricultural production and had brought a new wealth, but at considerable cost The autumn crops of millets and pulses, on which the majority of the population depended for its staple diet, were not adapted to artificial irrigation The new production was in sugar-cane, cotton, indigo, opium and wheat destined for the cities and the export trade The pressures to grow these more "valuable" crops frequently resulted in over-cropping of the good land while the poorer land was neglected and the traditional systems of well irrigation abandoned Over vast areas high water tables and excessive deposits of salts on the surface of the soil were brought about by bad irrigation practices and poor drainage, the latter often caused by the alignment of the newly constructed roads and railways When the droughts came the inferior soils could no longer be pressed into service to make up the deficiency in food grains and the mass of peasantry starved

On top of all this the new standard rent rates and the charges for irrigation water were imposed with a rigidity which took no account of the annual variations in harvest, in marked contrast to the flexibility shown by previous arrangements The problem of indebtedness became infinitely worse The government, despite its activities in the pursuance of law and order and its massive public works programme, stopped short on principle at interfering with social structure and the free flow of trade The *zamindars*, landlords under the new tenancy laws and responsible for collecting the government's 50% of the rent rate, soon found themselves insolvent and subject to compulsory sale of their land In the end, to avoid total collapse, the administration had to institute a system of debt release which allowed them to be reinstated Public works construction, rent rate assessments, and the operation of the legal machinery necessitated a growing bureaucracy which swallowed up almost all of the revenue, creating a vicious circle from which little progress emerged

The significance of this book is more than as an authoritative documentation of the agrarian conditions in one area during a brief period of history Today India is experiencing the first benefits of the so-called "green and blue revolutions" If these are to have a greater success than was achieved by the British administration of a hundred years ago, then more account will have to be taken of the ecological and sociological constraints to technological change In volume 2 of her work, Dr Whitcombe intends to extend her survey to the period from 1900 to independence, thus providing a full perspective against which to judge current plans and achievements

GORDON CONWAY

Cradle to Grave

Developmental Physiology and Aging. By P. S Timiras Pp x+692 (Macmillan New York, Collier-Macmillan London, February 1973) £9 95.

ENTHUSIASM over a textbook is sometimes justified, and this would seem to be the case here. Professor Timiras and her co-authors have produced a comprehensive study book on human development which would be welcome even if it were not unique in being the first to include a full discussion of ageing The ageing section alone is the most comprehensive and up-to-date gerontological text now available, so the enterprise would seem to be beyond praise Past attempts to summarize gerontology have been desultory, limited to fundamental biology or to pathology, and poorly integrated with the preceding study of maturation This one covers all physical aspects of the ageing process, demography included, and even has a chapter on the pharmacological attack on ageing The scope of this part of the work alone is remarkable It is of a standard and accuracy to appeal both to students, who are increasingly in need of gerontology teaching, and to experts

The quality of the developmental sections is similar, while the last half of the book is necessary information for the geriatrician, the first half is an orientation in paediatrics, human genetics and basic medical biology, excellently judged for medical and non-medical use The title is misleading in that developmental physiology is dealt with in detail in its own right, and not as a comment on age processes If it has a deficiency, in the light of the rate at which biology is widening, it is the self-imposed one of avoiding psychosocial biology, the section on sex determination, for example, contains no reference to learning and sex roles, and the opportunity of relating human rearing and psychosexual development to primatology and the peculiarities of the human growth curve has not been taken, but this is presumably a matter of policy Illustrations and tables are excellent, the index adequate, and the bibliographies mostly updated to 1970 or later The existence of this book should do a great deal both for gerontology and for the teaching of medical biology in general—it reflects the quality of the excellent grounding in these fields which Professor Timiras's course at Berkeley has been giving, and makes it generally available to teachers and students Its appearance here is most welcome

A COMFORT

Introducing Genetics

Genetics a Basic Guide By I J Pedder and E G Wynne Pp 183 (Hutchinson Educational London, December 1972) £1 90

AN introductory text for schools and colleges, such as this book claims to be, should aim to satisfy several basic requirements It should be stimulating, accurate, informative and easy to read Unfortunately this particular book fails to make the grade on several counts I found the style frequently pedantic and occasionally patronizing

The book has ten chapters which follow the fashionable sequence DNA, gene action, Mendel, linkage, sources of variation, mating systems, population genetics and applied genetics with a final chapter devoted to experimental methodology

The treatment of gene action is competent and informative, there is enough detail to stimulate but not too much to assimilate I think, however, that the problem of differential gene action in development warrants more than a single page of text, most of which is devoted to the *lac* operon The chapters on transmission genetics are well set out but would have been better with the inclusion of some examples for readers to work out for themselves It is a pity that the chapter on variation deals almost exclusively with chromosomal aberrations, allowing only one page for a very uninspired section on gene mutation Genes in populations is another topic which is covered well with plenty of relevant examples I am not sure that I like human genetics to be included under the umbrella of applied genetics, surely in a book at this level it merits a separate chapter The sections on plant and animal breeding are rather weak and will not convince many readers that genetics has practical relevance Why not mention the "green revolution"?

The book contains several unfortunate errors and omissions Twenty years after Watson and Crick it is inexcusable to diagram the double helix with chains of the same polarity and to indicate that it replicates by one half-helix acting as the template for a complementary strand, which is formed, apparently non-enzymatically, from a mixture of free bases and sugar phosphates In my opinion it shows extreme nomenclatural conservatism to refer to linkage and recombination as "non-Mendelian inheritance" The photographs of mitosis and meiosis are good but the reader should not be left to guess the identity of the organisms used to make the preparations Two other photographs are so poor as to be quite useless One, of maize pollen grains segregating for waxy/non-waxy, has been reproduced to give all the intermediate shades from black to pale-grey The other, which illustrates the segregation of black/white ascospores in *Sordaria fimicola*, does little justice to what is, or should be, an excellent demonstration of the segregation of the alleles of a single gene

There are cheaper books which cover less ground but do it better, and others, not much more expensive, which are more comprehensive and readable It may be significant that whereas the authors acknowledge sources of material and information there is no specific mention of anyone having edited or at least commented on the whole manuscript I wonder if anyone did

R A WOODS

Structured Programming

Structured Programming By O J Dahl, E W Dijkstra, and C A R Hoare Pp viii+220 (Academic New York and London, October 1972) £4 20, $12 50

CRITICISM, to me, carries a hint of superiority, and even an appreciation implies equality I make no such claims and I indulge in this impertinence only because so very few are qualified to review the work of Professor Dijkstra, whom the publishers correctly call "one of the leading programmers of the day"

Structural Programming comprises three competent useful articles about very large computer programs The first, a lucid presentation by Professor Dijkstra that is comprehensible given only a nodding acquaintance with programming, discusses some difficulties, particularly verification and proof, indicates mental aids which help in overcoming these, and suggests how a major program may be constructed Interestingly, this involves a restricted topology His process is highly structured, in many hierarchical levels of decreasing abstraction and increasing particularity, with minimal internal decision-making at each stage

This facilitates comprehension, proof and modification, but it seems at some cost in the complexity of the construction—though there is no simple way to design large programs He mentions the storage requirement/computation speed trade-off and illustrates grouping and sequencing in an elegant closing example Large-scale programming is still more art than science This note made it less so

The second section goes into some detail on the structure and storage of data, and on the assumptions and choices that underlie these It was illuminating and informative, yet I felt that it was wholly relevant only to a fairly high-grade specialist programmer

Finally, a short monograph deals largely with certain features of the powerful high-level language SIMULA 67—a fact which should be mentioned on the dust-jacket and in the abstract—and illustrates the implementation of some of the concepts introduced in the earlier sections

This book was irritating because it was too good to spoil ineptly These articles do have links but they are primarily useful to quite different groups and they should never have been published together The Dijkstra section will extend the understanding of almost anyone beyond the basic programming level, the rest is just not as general, and £4 20 is a lot for a single relevant part, particularly to the students and junior staff who most need it

NOEL FALCONER

Addendum

THE following bibliography was omitted from the book review "Space Science" by R L F Boyd (*Nature*, **243**, 483, 1973)

Space Research Physical and Technical Principles By M G Krishkin Translated from Russian Pp 314 (Jerusalem Israel Program for Scientific Translations, 1972) (Distributed by John Wiley and Sons, Ltd, Chichester) £9 65

Obituary

Dr E. Bretscher, CBE

Dr Egon Bretscher, who died suddenly in Zurich on April 16, had worked continuously on the British atomic energy project for longer than almost anyone else when he retired in 1966 as head of the Nuclear Physics Division at the Atomic Energy Research Establishment, Harwell His work before and after 1940 (when he became attached to the project) was especially wide ranging, covering both chemistry and physics, and pure and applied science

Born in 1901, the son of a Zurich banker, Bretscher's higher education was at the Eidgenossisch Technische Hochschule (ETH) in chemical engineering His continuing interest was organic chemistry and he went to Edinburgh to take his PhD Back at the ETH, Debye arranged an assistantship for him in the Physics Department, where he was one of the first people to use dipole moments to understand the chemical structure of an organic molecule In this period he met many of the famous physicists who came to work with Pauli He was a keen mountaineer and in 1930 he was rock climbing with Felix Bloch, who slipped down a vertical face, Bretscher saved Bloch's life—an exploit which he referred to later as his greatest contribution to physics

He was awarded, on the recommendation of Debye and Pauli, a Rockefeller Fellowship at the Cavendish Laboratory in Cambridge for the year 1934–35 Here he was introduced to Rutherford and nuclear physics He returned to Cambridge in 1936 where he stayed until January 1944, first as a Clerk Maxwell Scholar and then as a lecturer in experimental physics His physics was self-taught and his additional deep knowledge of chemistry, including radiochemistry, made him an experimentalist of "outstanding skill" (in A P French's words) and an especially valuable member of the Cavendish In the prewar period he concentrated on the supposed "transuranic" elements produced by bombarding uranium or thorium with neutrons, and (with N Feather) was one of the first in 1939 to identify the activity in question not as a "transuranic" element but as an unusual isotope of a common element, in this case $2\frac{1}{2}$ h iodine About the same time, with L G Cook, he demonstrated the recoil of fission fragments by collecting them on various surfaces

When the British Maud Committee began work in April 1940 to study the possibility of an atomic bomb, Bretscher was one of the physicists enlisted to help He made two notable contributions First, he wrote in December 1940 (with Feather) a report predicting that the new element 94, formed in the course of slow neutron reactions in uranium 238, would have a large fission cross section which would permit both the production of a super explosive mass and the use of uranium 238 for fission Bretscher worked out a method of isolating element 93 if sufficient irradiation of the uranium could be achieved and he felt he could do the same for 94 when minute amounts were available The Cambridge equipment, however, was too primitive for the necessary irradiation Bretscher's second contribution was to devise an ingenious technique for measuring the cross section of uranium for fast neutrons (*Nature*, **213**, 961 , 1967) In a different direction, he helped the late Dr D E Lea in the latter's study of the effects of radiation on biological specimens From work on the lethal action of radiation on the bacterium *Escherichia coli*, they concluded that bacteria, like higher organisms, have heritable genes and estimated the number of these genes to be somewhat greater than 1,000

Bretscher was one of the British atomic scientists sent early in 1944 to Los Alamos where he worked in Fermi's Advanced Development Division There, he was responsible for the "monstrously large" measurements of the deuterium tritium reactions which foreshadowed the hydrogen bomb

Bretscher returned to Britain and the newly created Harwell late in 1946 and thereafter became primarily a scientific administrator—first in temporary charge of the Chemistry Division and then, from 1948, as head of Nuclear Physics Although he had a profound respect for pure science, he urged that Harwell's chief task was to serve the practical needs of atomic energy by providing the engineers with scientific information for building the first production plants and then nuclear reactors An example of his practical gifts was the planning with H Seligman of the experiment called "Seanuts", which established the conditions governing dilution and dispersion of effluents discharged into the sea off the Cumberland coast, an operation which yielded valuable new scientific, as well as technical, information

Convinced that work of the Nuclear Physics Division should be directed to the needs of reactor design, Bretscher held the view—then heretical but now generally accepted—that reactors should be designed from first principles, given an adequate knowledge of the requisite nuclear constants His objectives were thus to systematize the requirements for nuclear data for reactors, to provide facilities for their measurement and to compile and evaluate the results of such measurements so that they were available in useful form In 1950 he set up and chaired the Nuclear Reactor Data Committee consisting of nuclear and reactor physicists and chemists, it produced exceptionally close collaboration between "users" and "measurers" In 1955, the Tripartite Nuclear Cross Section Committee was formed to foster collaboration between the UK, the USA and Canada Much of its success was due to Bretscher, who later chaired it He greatly influenced the drafting of its terms of reference, and his enthusiasm and foresight, coupled with authority and integrity, produced cooperation on a very large scale He was, *inter alia*, the first to recognize the practical importance of quantum effects in the slowing down of neutrons in reactor moderators and organized through the Committee a major collaborative effort on this By 1963 the capability of other Western European countries was such that the organization was expanded into the European American Nuclear Data Committee which Bretscher chaired Before his retirement he was on the organizing committee of the world-wide International Nuclear Data Committee

Meanwhile, under Bretscher, the Nuclear Physics Division built up its equipment into one of the most powerful ensembles for applied nuclear physics in the world Most notable among the machines used were the successively more powerful linear electron accelerators used as pulsed neutron sources, culminating in the — still unique — multiplying assembly known as the neutron booster The Nuclear Physics Division was, moreover, the birthplace of several activities which reached their full development elsewhere—for example, the work on neutron scattering in solids and liquids and on ion implantation

Bretscher's anxiety to maintain the highest scientific standards was seen lower down the professional scale Long before the Training Boards, he appreciated the importance of competent supporting staff for the scientists, and set up a Scientific Assistants Training School for youngsters straight from school and took a stimulating, personal interest in it

The variety and practicality of Bretscher's work, and the fact that some of the most important was done in war-time, meant that he did not always receive the scientific appreciation due to him He did not clamour for credit and never appended his name to papers published from Harwell

In 1931 he married Hanni Greminger, a very gifted mathematical student at the ETH, and they had five children, all three sons do research in the biological sciences His happiness with, and pride in, his family were the mainstays of his life

Announcements

University News

Professor A. Williams has been appointed to the Lapworth Chair of Geology and Headship of the Department of Geology at the **University of Birmingham**

Mr R K. Elliott, has been appointed to a Chair in the School of Education and to the Headship of the Division of History and Philosophy of Education at the **University of Birmingham**

Miscellaneous

Dr John C. Bowman has been appointed Director of the **Agricultural Research Council's Animal Breeding Research Organization.**

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Common Insect Pests of Stored Food Products a Guide to their Identification By Dr H E Hinton and Dr A Steven Corbet Fifth edition Pp 62 (Economic Series No 15) (London British Museum (Natural History), 1972) 50p [262

Civic Trust Awards 1972 County Borough and Large Burgh Areas Pp 100 (London Civic Trust 17 Carlton House Terrace SW1Y 5AW, 1973) 75p [262

The Natural Environment Research Council Publications Series B, No 4 Research in the Atmospheric Sciences Pp 23 Publications Series B, No 5 Marine Wildlife Conservation An Assessment of Evidence of a Threat to Marine Wildlife and the Need for Conservation Measures Pp 39 Publications Series C, No 9 The Severn Estuary and the Bristol Channel—An Assessment of Present Knowledge Pp 19 (London The Natural Environment Research Council, 1972 and 1973) [262

University of Cambridge Department of Applied Biology Memoir No 44 A summary of the papers published and research in progress by the members of the Department and its Associated Research Organisations during the period October 1st 1971–September 30th 1972 Review Series No 27 Biology as a Humanity Pp 24 (Cambridge The University, 1972) 15p [13

Forestry Commission Trees and People Pp 10 Booklet No 36 Timber Measurement for Standing Sales Using Tariff Tables By G J Hamilton Pp 31 14p Booklet No 38 Common Trees Pp 16 8p net Bulletin 46 Forest of Dean Day Visitor Survey An Analysis of the Demand for Day Visitor Facilities By Robert J Colenutt and Roger M Sidaway Pp vi+52+8 plates 60p net Forest Record 85 The Coal Tit By A J Deadman Pp 14 14p net (London HMSO, 1973) [13

The Association of Commonwealth Universities Annual Report of the Council, 1971–72 Pp 51 (London Association of Commonwealth Universities, 1973) [23

London School of Hygiene and Tropical Medicine (University of London), incorporating the Ross Institute and the TUC Centenary Institute Annual Report 1971/1972 Pp 34 (London TUC Centenary Institute of Occupational Health, 1973) [23

Computer Board for Universities and Research Councils Report of the Computer Board for the period 1st April, 1970–31st March, 1972 (Cmnd 5220) Pp 21 (London HMSO, 1973) 16p net [23

University of Strathclyde Annual Report, 1971/1972 Pp 84 (Glasgow University of Strathclyde, 1973) [23

Predatory Birds in Britain By the Avian Predators Working Party Pp 64 (London The British Field Sports Society, and The Council for Nature 1973) 36p. [23

Philosophical Transactions of the Royal Society of London B Biological Sciences Vol 264 No 865 The Secretion and Structural Evolution of the Shell of Thecodeidine Brachiopods By A Williams Pp 439–478+plates 40 to 53 £2 10 $5 90 Vol 264, No 866 An Ultrastructural Study of Axonal Changes Following Constriction of Postganglionic Branches of the Superior Cervical Ganglion in the Rat By Margaret R Matthews Pp 479–508+plates 54–62 £1 40, $3 90 (London Royal Society of London, 1973) [23

The Zoological Record, 1968, Vol 105, Section 13 Insecta, Compiled by the Staff of the Zoological Society of London Pp xi+747 (London The Zoological Society of London, 1972) [23

Loughton College of Further Education Prospectus 1973/1974 Pp 74 (Loughton, Essex Loughton College of Further Education, 1973) [53

The University of Leeds Publications and Titles of Theses, 1970/1971 Pp 145 (Leeds The University, 1972) 65p [63

The Carnegie United Kingdom Trust Fifty-ninth Annual Report 1972 Pp 24+13 photographs (Dunfermline, Fife The Carnegie United Kingdom Trust, Comely Park House, 1973) [63

Other Countries

Publications de l'Institut National pour l'Étude Agronomique du Congo Caractérisation Morphologique et Physico-Chimique de Profils Types de l'Afrique Centrale Par C Sys (Hors Serie) Pp 497 (Bruselles Institut National pour l'Étude Agronomique du Congo, 1972) 1,000 francs [262

Smithsonian Contributions to Zoology No 132 Morphology, Behavior, and Histogenesis of the Pelagosphera Larva of *Phascolosoma agassizii* (Sipuncula) By Mary F Rice Pp iii+51 (14 plates) $1 25 No 135 Freshwater Triclads (Turbellaria) of North America, V The Genus *Polycelis* By Roman Kenk Pp iii+15 45 cents No 138 Freshwater Triclads (Turbellaria) of North America, VI The Genus *Dendrocoelopsis* By Roman Kenk Pp iii+16 45 cents Smithsonian Contributions to Paleobiology, No 14 Permian Branchiopods of West Texas, I By G Arthur Cooper and Richard E Grant Pp 230 (23 plates) $2 25 (Washington, DC Smithsonian Institution Press, 1972 and 1973) [262

Girard Estate Coal Lands in Pennsylvania, 1801–1884 By John N Hoffman (Smithsonian Studies in History and Technology, No 15) Pp 86 (Washington, DC Smithsonian Institution Press 1972) [262

Australian Journal of Botany, Supplementary Series No 6 The Palynology of Some Tertiary Pleistocene Deposits, Lachlan River Valley, New South Wales By Helene A Martin Pp 57 (East Melbourne Editorial and Publications Section, CSIRO, 372 Albert Street, 1973) [13

Australia Department of Supply Defence Standards Laboratories Annual Report, 1971/1972 Pp 87 (Ascot Vale, Victoria Chief Superintendent Defence Standards Laboratories, 1972) [13

Rubber Research Institute of Malaya Annual Report 1971 Pp 168 (Kuala Lumpur Rubber Research Institute of Malaya, 1972) $3 [13

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Population Bulletin, Vol 28, No 4 Abortion—the Continuing Controversy Pp 1–32 (Washington, DC Population Reference Bureau, Inc , 1972) 50 cents [13

The International Nickel Company of Canada Ltd 1972 Annual Report Pp 32 (Sudbury, Ontario The International Nickel Company of Canada Ltd , 1973) [13

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DIFFERENTIATION is a new bi-monthly journal devoted to the problem of biological diversification. Papers in this journal will focus on the differentiation of eukaryotes at the molecular level but the ambition of the journal is to cover biological differentiation and evolution from the sub-cellular level to species differentiation. The Editors would welcome contributions.

The first issue of DIFFERENTIATION will be published in January 1973. The first issues will include the following representative articles.

Time-lapse filming of cellular interaction in organ culture. Paper 1: Behaviour of non-malignant cells.
E. J. Ambrose and D. N. Easty

Studies of the effects of bromodeoxyuridine (BUdR) on embryonic differentiation.
J. Brachet, R. Tencer and M. Engelhart

Evidence for the presence of a readily transmissible oncogenic principle present in crown gall teratoma tissues of tobacco.
F. Meins

Histochemical features of neural induction in *Xenopus laevis.* D Tarin

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30

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APPOINTMENTS VACANT

Research Technician Drug Metabolism

We are a leading U K Pharmaceutical Company based at Degenham, Essex, and are seeking a Research Technician to assist in studies on the metabolism of new medical products

Candidates should possess a knowledge of analytical biochemistry, preferably with experience in instrumentation and techniques associated with the study of drug metabolism in animals and man

Salary is dependent upon age and experience

Please apply in writing giving brief details of age, and experience to the Personnel Manager, May & Baker Ltd , Dagenham, Essex RM10 7XS quoting reference No 222/N/73

M&B May&Baker

(66)

SCHOOL OF AGRICULTURE ABERDEEN

Applications are invited for the new post of LECTURER IN AGRICULTURAL ZOOLOGY (PARASITOLOGIST) Preference will be given to candidates with a degree in agriculture with postgraduate experience in animal parasitology or a related science degree combined with a sound knowledge of agriculture

Appointment will be made to one of the following scales

Grade III	£2,176-£3,795
Grade IV	£1,462-£2,007

with entry according to qualifications and experience

Medical examination Superannuation scheme

Further particulars and forms of application (Reference Number 49/73) may be obtained from the Secretary, The North of Scotland College of Agriculture, School of Agriculture Building, 581 King Street, Aberdeen AB9 1UD, with whom application should be lodged **not later than August 31, 1973**

(8)

Toxicology Research

The Toxicology area of our Research Department, situated in modern, well-equipped laboratories in Nottingham, continues to expand as more projects reach advanced stages of investigation and new projects are initiated Two new opportunities have been created for biological scientists to join the team engaged in the safety evaluation of new medical, animal health and crop protection products —

Reproduction Toxicologist

will assume responsibility for all reproduction and teratological investigations and, additionally, will contribute towards technical documents for product registration in the U K and overseas Publication of results and attendance at scientific meetings are encouraged Applications are invited from good honours graduates in a biological science possessing relevant postgraduate experience (Ref U 148/1)

Non-Medical Clinical Biochemist

will plan, develop and maintain new assay procedures Applicants should be keen to innovate and, desirably, have experience of clinical biochemistry in hospital or industrial laboratories (Ref U 148/2)

Conditions of employment are attractive and include good profit sharing and contributory pension schemes Some help with relocation expenses will be granted where appropriate

Please write, giving brief details of age, qualifications and experience to — J F Pattison,

Boots The Boots Company Ltd.
Station Street Nottingham NG2 3AA.

(118)

UNIVERSITY OF DUBLIN
Trinity College

CHAIR OF PHYSICS

The Erasmus Smith Chair of Natural Philosophy (founded 1724) will fall vacant in October 1974 following the retirement of the present holder, Dr E T S Walton

Persons interested in this appointment should write for further particulars to

The Secretary to the College,
Trinity College,
Dublin 2

(122)

Medical Research Council

SCIENTIST

Scientist required for the Secretariat of the Committee on Protection against Ionising Radiations Duties include the reporting and organising of meetings, appreciation of current literature on a wide variety of topics in biology, medicine, and physics There would be opportunities for relevant experimental work The successful candidate would be located at the Radiobiology Unit at Harwell and would enjoy M R C salary scale and conditions of service

Applications should be addressed to The Administrator, M R C Radiobiology Unit, Harwell, Didcot, Berks , to reach him by August 15, 1973 Please quote reference FDB/33 (87)

Imperial Chemical Industries Limited
Agricultural Division
Jealott's Hill Research Station, Bracknell, Berkshire.

ANIMAL NUTRITION

Animal nutrition research activities at Jealott's Hill are expanding both in the ruminant and non-ruminant area New products have recently been introduced to the market and it is confidently expected that these will be added to in the near future as a result of current research activities Due to this increasing activity, vacancies exist for

Non-Ruminant Nutritionist

A major ICI development is in progress at present and recently reaching the pilot plant scale is the production of single cell protein using methanol as the carbon source Over the next few months the quantity of product available will move from the tons per annum scale to hundreds of tons per annum The existing research programme is therefore being radically increased to involve long-term and large-scale testing of the product with pigs, poultry and veal calves

In addition to the increased nutritional work within the Company at Jealott's Hill, trials will be arranged with other relevant Research Institutes, Animal Feedstuff companies, etc, both in the UK and abroad, particularly in Europe

To assist in this rapidly increasing Research/Development programme, a Nutritionist with particular interest in pig nutrition will be recruited The successful candidate is likely to be a graduate with a number of years of relevant research experience in the nutrition of non-ruminant animals, preferably with a specific interest in either pig or veal calf nutrition He will be expected to rapidly assume full responsibility for the pig nutrition programme at Jealott's Hill and for selecting and liaising with work at all outside centres

Ruminant Nutritionist

Research in forage conservation and other areas of ruminant nutrition is expanding and has led to the recent successful introduction of products such as "Sylade" to the market in the UK Both commercial and research activity in this area is likely to expand in the future leading to a greater ICI involvement in the areas of agriculture both in the UK and Europe generally

A graduate in an agricultural science subject, such as animal biochemistry, with a particular interest in ruminant nutrition, is required to initiate and carry out trial work with dairy cows, beef cattle and related metabolism trials with sheep, goats, etc The successful candidate is likely to have had some years' experience of nutritional work of this type and be able to rapidly fit into and contribute to the work of the existing team of nutritionists, biochemists and microbiologists Although the work is centred on Jealott's Hill, trials are carried out on other Company farms in the UK and some travel abroad is likely to initiate and progress trials in Europe at relevant research centres

Jealott's Hill is the location of much of ICI's agricultural research and is situated in pleasant countryside thirty-five miles west of London within easy reach of varied and attractive residential areas

The Company operates House Purchase, Profit Sharing and Contributory Pension schemes and offers financial assistance towards removal expenses for married men

Write, giving brief details of age, qualifications, experience, etc , to

M A J W Pegg
Personnel Department
Imperial Chemical Industries Limited
Agricultural Division
PO Box No 1
BILLINGHAM
Teesside

(112)

HOECHST PHARMACEUTICALS RESEARCH LIMITED

HEAD OF ADMINISTRATION

Hoechst, one of the largest chemical companies in the world, is building a new Pharmaceutical Research Centre at Milton Keynes in Buckinghamshire which will become operational in early 1974 The Research Director would welcome applications for the senior post of Head of Administration to work closely with him to create and then manage an administrative system for the laboratories

Responsibilities

To establish administrative systems and forward planning techniques, liaising with Hoechst UK Management, in particular, on systems relating to financial monitoring, and with our German Parent Company on research planning data handling and information retrieval systems.

To advise the Research Director on major capital expenditure items, and to act as Chairman of the Centre's Finance and Building Committee

To co-ordinate meetings and reports and to compile quarterly reports

To supervise the work of the Laboratory Manager and the Technical Information Officer

Qualifications

Applicants should have had administrative experience at a policy-making level in an organization with a high proportion of graduate scientific staff

Knowledge of the German language and Systems Analysis would be valuable

An attractive salary will be offered The company also operates a merit bonus scheme, and free membership for employees and dependants of the PPP Health Scheme

The pension scheme is contributory Assistance with house removal is also available

Would applicants in the first instance write, with fullest possible details, to
Pharmaceutical Division, Hoechst UK Ltd ,
Hoechst House, Salisbury Road, Hounslow, Middx TW4 6JH
Tel 01-570 7712, Ext 3082

(121)

Department of the Environment
Water Pollution Research Laboratory, Stevenage

CHEMISTS/ CHEMICAL ENGINEERS

Two posts in a team which is developing advanced methods of treating municipal waste waters Each is likely to involve a period of secondment to a 100,000 gal/day plant planned for Coleshill, Staffs, one (Post A) as Assistant Project Manager, the other (Post B) as Chief Analyst.

Post A. Candidates, aged 25–32, must have a 1st or 2nd class honours degree in Chemical Engineering or a related subject and several years' experience of pilot plant and development work, preferably in the waste water field Appointment will be as Higher Scientific Officer (£2,076–£2,667) or Senior Scientific Officer (£2,615–£3,640), according to age and experience Ref SA/5/HE

Post B. Candidates, under 30 years of age, must have a 1st or 2nd class honours degree in Chemistry, together with experience in the analysis and treatment of waste waters Appointment will be as Higher Scientific Officer (£2,076–£2,667) Ref SA/6/HE

Application forms (to be returned by 24 August 1973) available from The Director, Water Pollution Research Laboratory, Elder Way, Stevenage, Herts RG2 1TH Please quote appropriate reference (30)

UNIVERSITY OF READING

TEMPORARY LECTURER IN GEOGRAPHY

Applications are invited for a Temporary Lectureship in Geography for a period of one year from October 1, 1973 The Lecturer will be required to teach courses in cartography, surveying, and hydrology The salary will be in the region of £2,500

Further particulars may be obtained from the Registrar (Room 208, Whiteknights House), The University, Whiteknights, Reading RG6 2AH, by whom applications should be received not later than August 18, 1973 (61)

UNIVERSITY OF SHEFFIELD

DEPARTMENT OF HUMAN BIOLOGY AND ANATOMY

LECTURER required, preferably with special interests in Human Biology, Anthropology or related fields Candidates should be capable of teaching topographical anatomy to medical and dental students

Applications should be sent to the Registrar and Secretary, The University, Sheffield S10 2TN, by August 21, 1973 Further details may be obtained by writing informally to Professor R Barer Quote Ref R 53/G (10)

UNIVERSITY COLLEGE HOSPITAL/ UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

SENIOR LECTURER MEDICAL PHYSICS DEPARTMENT

Applications are invited for the newly created post of Senior Lecturer in the joint Hospital and Medical School Department of Medical Physics The appointee will be responsible to the Director of the Department for the organisation of academic medical physics and the direction of a number of research projects concerned with in-vivo blood gas analysis Experience in this field is essential Salary will be in the range £4,143 to £5,247 plus £162 London Weighting

Further information about this post can be obtained from the Director, Medical Physics Department

Applications, with the names of two referees to

The Secretary,
U C H Medical School,
University Street,
London WC1E 6JJ

Closing date for applications August 31, 1973

(54)

UNIVERSITY COLLEGE, DUBLIN

DEPARTMENT OF PHARMACOLOGY

ASSISTANT LECTURER OR COLLEGE LECTURER

Applications are invited for an Assistant Lectureship or College Lectureship tenable from October 1973 Non-medical or non-veterinary candidates must have a Ph D in either pharmacology or physiology The Department has recently introduced science courses and caters particularly for biochemical, A N S , clinical and bio-engineering research interests

Salary scale

Assistant Lecturer £2,195 by £122 to £3,049

College Lecturer £3,232 by £154 to £3,386 by £148 to £3,534 by £140 to £4,234

Initial placing according to qualifications and experience Family allowances are payable The appointee may benefit from either a non-contributory or F S S U -type pension scheme

For further information, write to the Head of the Department of Pharmacology, University College, Foster Avenue, Blackrock, County Dublin, to whom applications (in triplicate) should be sent before August 24, 1973 These should name three referees and indicate age, qualifications and experience (39)

IMPERIAL COLLEGE

Interactions Between Adsorbed Atoms

Postdoctoral Research Assistantship for S R C-sponsored studies by field ion microscopy or atomic processes in thin film nucleation Experience of techniques used in clean-surface studies desirable Starting salary £2,091 per annum with F S S U Available for two years from October 1, 1973

Further particulars from Dr D W Bassett, Department of Chemistry, Imperial College, London SW7 2AY (124)

HAILE SELLASSIE I UNIVERSITY

ETHIOPIA

Applications are invited for the following posts in the Faculty of Medicine

CHIEF TECHNICIAN IN THE BASIC MEDICAL SCIENCES Applicants must have had at least 7 years' experience in one or more of the following disciplines Physiology, Biochemistry, Pharmacology They must also hold the Advanced Certificate of the City and Guilds of London Institute or equivalent Appointee will be responsible for co-ordinating the technical work of the 4 preclinical departments, organising and conducting courses for Ethiopian trainee technicians and administrative duties connected with ordering and purchasing of all equipment and supplies

SENIOR TECHNICIAN IN ANATOMY/HISTOLOGY Applicants must have had at least 5 years experience in an Anatomy or Histology Department and possess the Advanced Certificate of the City and Guilds of London Institute or equivalent Appointee will be responsible for supervising and assisting the technical work of the Anatomy Department, including the preparation of anatomical specimens and histological material, and with the training of Ethiopian technicians in these subjects

Appointments will be for 2 years in the first instance, renewable Salary scales Chief Technician Eth $16,400-Eth $20,000 per annum, Senior Technician Eth $14,000-Eth $16,400 per annum Salaries are tax free (£1 sterling=$5 5) Housing allowance (Eth $400 per month for married man with 2 children) Family passages and baggage allowance

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail not later than August 29, 1973, to the Dean, Faculty of Medicine, Haile Sellassie I University, P O Box 1176, Addis Ababa, Ethiopia Applicants resident in U K should also send one copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT Further particulars may be obtained from either address (48)

UNIVERSITY OF MANCHESTER

POSTDOCTORAL RESEARCH ASSOCIATE IN CYTOGENETICS

Applications are invited for this post in the Department of Zoology to work on an S R C sponsored project concerned with chromosome studies of the yellow-fever mosquito *Aedes aegypti* with special reference to meiotic drive Candidates acquainted with polytene chromosome analysis preferred Post tenable for three years from October 1, 1973 Starting salary £1,764 rising to £2,079 per annum F S S U

Further particulars and application forms (returnable by August 10) from the Registrar, The University, Manchester M13 9PL Quote ref 133/73/Na (7)

UNIVERSITY OF LEICESTER

LECTURERS IN GEOLOGY

Applications are invited for two Lectureships in the Department of Geology

(a) **Lectureship in Geophysics**—applicants qualified in any aspect of geophysics will be considered

(b) **Lecturer in Economic Geology**—a knowledge of mining engineering and surveying would be advantageous, as would some industrial experience graduates in geology, mining geology and mining engineering will be considered

Salary according to qualifications and experience on scale £1,929 to £4,548 per annum, with F S S U membership

Further particulars from the Registrar, to whom applications should be sent by August 31 (6)

Wellcome

Drug Metabolism

Applications are invited from graduates for newly created opportunities of different seniority in the Department of Drug Metabolism for research into the scientific development of new drugs

Candidates should have a good first degree, probably in biochemistry or chemistry, they should also have profited from some years' practical experience in the study of drug metabolism either through working successfully for a Ph D degree, through post-graduate employment, or through both An extensive knowledge of modern techniques and methodology is essential

The Department is very well equipped and there is ample opportunity for interaction with workers in other disciplines In addition to the investigation of specific compounds members of the Department are encouraged to pursue research at a more fundamental level and to publish their results

The laboratories are situated in pleasant parkland surroundings within easy reach of Bromley, London and Croydon, and general conditions of employment are excellent

Applications, giving brief details of relevant experience, should be sent to **The Personnel Manager,**
THE WELLCOME RESEARCH LABORATORIES,
Langley Court, Beckenham, Kent.

(68)

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

VACANCY IN THE FEEDING AND METABOLISM DEPARTMENT

A research scientist is required to investigate the flow of intestinal digesta in dairy cattle The immediate responsibility is to continue the development of apparatus for measurement and sampling of digesta passing through the duodenum, an apparatus is at the prototype stage There will be a continuing responsibility for supervision of the application of the technique in important collaborative studies involving a number of other workers In parallel to these duties the successful candidate will be encouraged to develop his own line of work into an aspect of gastrointestinal function revelant to the programme of the department

Applicants should have a 1st or upper 2nd class honours degree in physiology, biochemistry, or veterinary or agricultural science and postgraduate experience involving duodenal cannulae or other aspects of gut function

Appointment would be in the grade of Higher Scientific Officer (£2,076 to £2,667) or Senior Scientific Officer (£2,615 to £3,640), depending on qualifications and experience A non-pensionable allowance of 4½% of basic salary will be paid to offset contributions under F S S U arrangements Application forms are obtainable from the Secretary, NIRD, Shinfield, Reading RG2 9AT Quote reference 73/24 (41)

UNIVERSITY OF LIVERPOOL

DEPARTMENT OF HISTOLOGY AND CELL BIOLOGY (MEDICAL)

Applications are invited for the post of SENIOR DEMONSTRATOR in the Department of Histology and Cell Biology (Medical) The post is tenable from October 1, 1973

The post is suitable for a graduate in Physiology, Biology or Biochemistry, possessing a Ph D, who wishes to gain teaching experience whilst continuing with research

The appointment, for a year in the first instance, will be on the salary scale £1,959 to £2,055 to £2,178 per annum

Applications, together with the names of three referees, should be received not later than August 21, 1973, by the Registrar, The University, P O Box 147, Liverpool L69 3BX, from whom further details may be obtained Quote Ref RV/N/80396 (5)

GUY'S HOSPITAL MEDICAL SCHOOL

Junior Technician/ Technician

required in Biology Department for a parasitology laboratory concerned mainly with degree teaching Duties include preparation of slides, material, etc, and assisting with general departmental duties, including research

Apply, in writing, stating age and giving details of education, qualifications and experience, and quoting Ref B.D 1, to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT (63)

UNIVERSITY OF SURREY

DEPARTMENT OF CHEMICAL ENGINEERING

WORKSHOP TECHNICIAN

£1,538 to £1,794

Applications are invited for a Workshop Technician to assist in the construction of equipment and components for research and teaching purposes from engineering drawings, sketches and verbal instructions An all-rounder is needed who will be required to perform a variety of tasks, some of which will involve work on machine tools Workshop training and between 3 to 5 years' experience in techniques such as milling, drilling, grinding, planing, soldering and brazing essential

STORES TECHNICIAN

£1,723 to £2,028

Stores Technician required for the administration and supervision of the Departmental general stores for engineering tools and materials scientific equipment and chemicals Between 6 to 7 years' experience in one of these fields is essential

Both positions are permanent, superannuation scheme

Application forms may be obtained from the Assistant Secretary (Personnel), University of Surrey, Guildford, Surrey GU2 5XH, or telephone Guildford 71281, Ext 452, and to whom they should be returned to by August 10 (71)

The Natural Environment Research Council

Director

Institute of Terrestrial Ecology

The Natural Environment Research Council invites applications for the post of DIRECTOR of the INSTITUTE OF TERRESTRIAL ECOLOGY.

This new Institute incorporates the research staff and facilities which have hitherto comprised the Research Branch of the Nature Conservancy It will have two inter-related tasks One will be to advance, with funds from the Science Budget, the science of terrestrial ecology and related disciplines Emphasis will be given to observing and interpreting ecological pattern, change and stability, and investigating their underlying causes and processes, both to add to basic knowledge and to lay a sound scientific basis for practical conservation and environmental management in the years ahead The other task will be to provide applied research and services commissioned by the Nature Conservancy Council or by other organisations in the fields of conservation and ecology

The Director of ITE will be expected, under the guidance of Council and in conjunction with Council Headquarters, to provide scientific leadership of the highest calibre in furthering the work of the Institute. He will be assisted by a Deputy Director, whose duties will include special responsibilities for administration and co-ordination of commissioned research over the whole field, and a small executive group

It is intended that the Director and the majority of this central Directorate will be based at the Monks Wood Experimental Station, Huntingdonshire The total staff of the Institute number about 250 and are stationed in several laboratories in England, Scotland and Wales

The post of Director of the Institute of Terrestrial Ecology carries the rank of Chief Scientific Officer (B) with a salary at present of £7930 p a

Superannuation arrangements

Closing date 31 August 1973

Application forms and further particulars may be obtained from Mr J H Morton,
Establishment Division,
The Natural Environment Research Council,
Alhambra House,
27/33 Charing Cross Road,
London WC2H 0AX

(110)

JUNIOR TECHNICIAN REQUIRED for the Electron Microscope suite of the Department of Neuropathology Previous experience is desirable but not necessary as full training and day release is given Salary and conditions in accordance with Whitley Council scales—Applications from the Secretary, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, quoting reference PMD/N (73)

TECHNICIAN with some experience in histopathology required to work for 12 months in the Max Planck Institute, Frankfurt, Germany This is an interesting post involving mainly research on the primate central nervous system Applicants should get in touch with Professor P M Daniel, Department of Neuropathology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, quoting reference PMD/N (114)

UWIST
CARDIFF
University of Wales Institute of Science and Technology

PROFESSOR

OPHTHALMIC OPTICS

Salary within professorial range

Requests (quoting Ref Na/R8/Ga-4/117) for details to Personnel Section, UWIST, Cardiff CF1 3NU Applications to be received by August 24, 1973 (13)

PORTSMOUTH POLYTECHNIC

DEPARTMENT OF MATHEMATICS

RESEARCH ASSISTANTSHIP IN CONTROL TECHNOLOGY

Applications for the above post are invited from first or second class honours graduates in Mathematics, Science or Engineering, with a special interest in Stochastic Processes and/or signal analysis The successful candidate will be expected to work for a higher degree and will be encouraged to publish his results

Salary scale £1,120 to £1,220 per annum

Application forms and further particulars may be obtained from Dr J K Hammond, Department of Mathematics, Portsmouth Polytechnic, Hampshire Terrace, Portsmouth PO1 2EG, to whom completed applications should be returned by August 20, 1973

(106)

MONASH UNIVERSITY

MELBOURNE, AUSTRALIA

DEPARTMENT OF BIOCHEMISTRY

SENIOR TEACHING FELLOW

Applications are invited from postdoctoral science graduates preferably with undergraduate training in Biochemistry Enquiries from candidates in the process of completing their Ph D's would be welcome Appointees would be expected to commence duty early in 1974 The position involves limited teaching and appointees will participate in research programmes concerned with either

1 Cellular aspects of the action of growth hormone—under Professor J Bornstein (or)
2 Studies in the cathepsin like enzymes attacking articular cartilage components—under Professor D A Lowther

Salary range Senior Teaching Fellow $A7,270 to $A8,698 per annum

Benefits Travelling expenses for appointee and family, removal allowance, repatriation after three years' appointment if desired, temporary housing for an initial period

Further general information including details of application procedure is available from the Academic Registrar, Monash University, Wellington Road, Clayton, Victoria 3168, Australia, or the Secretary-General, Association of Commonwealth Universities (Appts) 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572) Enquiries to Professor D A Lowther, Chairman, Department of Biochemistry, in the University

Closing date September 17, 1973

The University reserves the right to make no appointment or to appoint by invitation (115)

QUEEN MARY COLLEGE

UNIVERSITY OF LONDON

DEPARTMENT OF ZOOLOGY AND COMPARABLE PHYSIOLOGY

Applications are invited for a Lectureship from October 1, 1973, or as soon thereafter as possible Preference will be given to candidates with interests in Ecological or Physiological aspects of fresh water biology

Salary scale £1,923 to £4,548 per annum, plus £162 London Allowance F S S U membership Application forms and further details from The Registrar (N), Queen Mary College Mile End Road, London E1 4NS, to be returned by August 22 (32)

Soil Surveyor

OVERSEAS ASSIGNMENTS

Bookers Agricultural and Technical Services manage sugar estates and undertake a wide range of international consultancy work in this and allied fields Its activities are expanding rapidly The Booker Group with assets exceeding £60 million has some 30,000 employees

An additional soil surveyor is now required to carry out soil and land capability studies overseas The work, often in difficult physical conditions, is demanding, and considerable travel is involved

Candidates aged 25 to 32 and preferably single should have a good first degree in natural sciences They should have specialised in soil science or alternatively have relevant post-graduate training Previous field experience ideally overseas, is highly desirable

The starting salary appropriate to qualifications and experience will be attractive Fringe benefits are excellent

BOOKER
McCONNELL
.LIMITED

Please send brief career and personal details, quoting reference U 22 to

V Mortensen,
Bookers Agricultural and
Technical Services Limited,
Bucklersbury House,
83 Cannon Street, London, EC4N 8EJ (90)

UNIVERSITY COLLEGE
GALWAY

PROFESSORSHIP OF PHARMACOLOGY

(within the Department of Experimental Medicine and Practical Pharmacology)

Applications are invited for the above statutory, whole-time post Salary scale £4 827 by £123 (8) to £5,811, plus Family Allowances Non-contributory Pension Scheme

The closing date for receipt of applications is October 1, 1973 Prior to application, further information should be obtained from the Registrar of the College (X80)

SOUTHMEAD HOSPITAL, BRISTOL

A GRADUATE IN BIOCHEMISTRY

preferably with some clinical biochemistry experience, is required to join a small team concerned with the screening and investigation of inherited metabolic disorders The primary responsibility of the successful candidate would be to develop methods and provide a service for the prenatal detection of these conditions A good knowledge of enzyme and radioisotope techniques would be particularly useful There would be good opportunities to work for further qualifications

For further details contact Dr J B Holton in the Biochemistry Department

The appointment will be made within the basic grade biochemists scale, salary £1,566 to £1,980 per annum, according to qualifications and experience

Application forms can be obtained from the Group Secretary Southmead Hospital Bristol BS10 5NB, and should be returned before September 8 (85)

Civil Aviation Authority

Ornithologists

■ **Two posts in small team** ■ **Study birds in Maplin area in connection with possible hazards at proposed airport** ■ **Considerable field work in all weathers.**

☐ Degree in Biology, Zoology or equivalent ☐ Practical knowledge of ornithology ☐ Driving ability essential ☐ Age under 27 ☐ Appointment (initially for 3 years) as Scientific Officer (£1318 – £2177) ☐ Ref SA/2/M ☐ Closing date 24 August 1973.

☐ Application forms from Department of Trade and Industry, E(P)3A Room 405, Savoy Hill House, Strand, London WC2 ROBX

(42)

Science group
CIVIL SERVICE

ASSISTANT PLANT BREEDER WANTED

To take charge of Amenity Grass Breeding programme and Evaluation of Cereal Varieties at an advanced breeding stage

Qualifications required a good knowledge of grass breeding methods, if possible in amenity grasses, ability to design and lay out trials and analyse the results obtained Knowledge of cereal variety evaluation would be an advantage, but not essential

It should be appreciated that the breeding work involved is specifically aimed at the production of new varieties rather than fundamental research into plant breeding problems

Applications should be made to Managing Director, Sinclair McGill Limited, P O Box 23, 67 Kyle Street, Ayr KA7 1RY, from whom further information is available if required (43)

UNIVERSITY OF EDINBURGH

DEPARTMENT OF BIOCHEMISTRY

Applications are invited for a post of RESEARCH ASSISTANT from graduates in biochemistry or related subjects for an M R C -sponsored post to work on the action of pancreatic hormones on liver cells The appointment is for three years from October 1, 1973 and there is possibility of registration for a higher degree

Salary scale £1,659 to £2,346 per annum

Applications, by letter, together with curriculum vitae and the names of two referees, should be sent to Dr D R Langslow, Department of Biochemistry, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG, not later than August 8, 1973

Please quote Reference 5061 (50)

CSIRO

AUSTRALIA

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas The Organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia

SENIOR RESEARCH APPOINTMENTS

DIVISION OF FISHERIES AND OCEANOGRAPHY

GENERAL The Division has a staff of over 40 scientists investigating the fisheries resources and the physical chemical and biological features of the oceans Headquarters of the Division is located at Cronulla, Sydney, and the Division has laboratories in Perth and near Brisbane

As a result of a recent reappraisal of the Division's research objectives, greatly increased emphasis will be given to fisheries programmes and to studies of estuarine and close inshore waters, particularly in relation to the environmental effects of man's activities It is intended that these studies should be of a broad interdisciplinary nature and take a systems approach to the problems including both the physical processes involved and their relation to the biological communities The great length of the Australian coastline and the diversity of climatic conditions offer a wide variety of estuarine types and associated problems

GROUP LEADERS

CRUSTACEAN BIOLOGY · FISH BIOLOGY (Ref. No 320/497)

DUTIES Two positions have been created for senior scientists to take charge of major sections of the Division's fisheries programmes They will be responsible to the Chief of the Division for the scientific effectiveness of the programmes under their charge and for associated administrative matters They will advise on the overall planning of the Division's programmes and on budgeting needs and allocations They will also ensure that these segments are properly executed and reported They will be required to co-operate with the heads of other groups in the Division in the planning and execution of multi-disciplinary projects, and with Commonwealth and State fisheries authorities in joint research and in advising on the management implications of research results

One appointee will be responsible for the programmes concerned with Crustacea These, mainly prawns and rock lobsters, at present constitute the largest segment of Australian fisheries with a landed value of about $A70,000,000 Present studies include major projects on the general biology and population dynamics of rock lobsters in Western Australia and of prawns along the east and north coasts from Moreton Bay, Qld , to Nickol Bay, W A , as well as studies of the physiology and behaviour of the principal species An early responsibility of the appointee will be to bring about closer integration of these programmes At present 13 scientists and about 20 technical staff are employed in the group

The other appointee will be responsible for the programmes dealing with fish resources Although programmes are on a relatively small scale at present, substantial expansion in this area is anticipated, and this development will be the primary responsibility of the appointee Initially, emphasis is likely to be given to the pelagic fisheries of the south-east Australia area, which seem likely to expand rapidly in the near future One major project in connection with these fisheries is just being commenced It is planned to expand the group quite rapidly to 4 or 5 scientists plus 20 technical staff

The appointees will be located at Cronulla

QUALIFICATIONS Applicants should have substantial records of independent biological research in relation to fisheries, including a significant period involving responsibility for planning and operation of programmes and control of research staff Experience in crustacean and pelagic fisheries would be an advantage for the respective positions

RESEARCH SCIENTIST

ESTUARINE ECOLOGY (Ref. No. 320/496)

DUTIES The appointee will take a leading role in the programme and, in particular, will provide a co-ordination between the scientists working in specialised disciplines, including physical and biological oceanography, who will be involved in the study The appointee will be required to select areas of study and develop research strategy In general, emphasis will be given to increasing understanding of the basic features of estuarine systems rather than to direct study for problem situations

The appointee will be located at Cronulla

QUALIFICATIONS Applicants should have substantial records of independent research in relevant fields with demonstrable ability to take a broad approach to the study of estuarine and similar systems Applicants should also have the ability to co-ordinate the work of other scientists in joint inter-disciplinary projects

SALARY The appointments will be made within the ranges of Principal Research Scientist or Senior Principal Research Scientist $A13,468–$A18,104 p a

TENURE Indefinite or fixed term appointments may be negotiated An indefinite appointment carries Commonwealth Superannuation benefits

APPLICATIONS Applications stating full personal and professional details, the names of at least two professional referees, and quoting the appropriate reference number should reach — **The Personnel Officer, Australian Scientific Liaison Office, 64–78 Kingsway, LONDON, WC2B 6BD**

by the 31st August, 1973

Applications in U S A and Canada should be sent to **The Counsellor (Scientific), Embassy of Australia, 1601 Massachusetts Avenue, N W , WASHINGTON, D C 20036, U S A**

(70)

THE QUEEN'S UNIVERSITY OF BELFAST

LECTURESHIP IN MARINE BIOLOGY

This post is tenable at the Marine Biology Station, Portaferry, from October 1, 1973 or such later date as may be arranged The appointment will be subject to a period of probation of up to three years Initial placing, which will depend on qualifications and experience, will be made at one of the first three points on the lecturers' scale £1,764-£1,923-£2,079 rising to £4,299 with F S S U

Applications should be received by August 18, 1973 Further particulars may be obtained from The Senior Assistant Secretary (Personnel), The Queen's University of Belfast BT7 1NN, Northern Ireland (Please quote Ref 73/N)

(22)

UNITED BRISTOL HOSPITALS

Applications are invited from science graduates for the post of

RESEARCH ASSISTANT

(basic grade hospital biochemist) in the Chemical Pathology Department of the United Bristol Hospitals (Royal Infirmary branch) The work will involve the investigation of plasma lipids in connection with a health screening programme The tenure of the post will be one year in the first instance, but may be extended for a further two years

Previous experience of hospital biochemistry is desirable but not essential Starting salary not less than £1,278 (£1,566 for first or second class Honours), with increments according to qualifications and experience

Applications, with the names of two referees, to Dr G K McGowan, Department of Chemical Pathology, Royal Infirmary, Bristol BS2 8HW

(59)

FACULTY OF MEDICINE, MEMORIAL UNIVERSITY OF NEWFOUNDLAND

Applications are invited for the position of ASSOCIATE DEAN of BASIC MEDICAL SCIENCES at Memorial University in St John's, Newfoundland

The person appointed would be expected to assist in developing the general policies and areas of emphasis of the Medical School and, in particular, the Basic Sciences, ensuring that these policies are reflected in faculty recruitment and other activities Preference will be given to candidates who have had considerable research and administrative experience

The duration of the appointment will normally be for a period of three years The post will carry an appropriate academic rank and tenure in accordance with university regulations Salary will be according to qualifications and experience

Applications, accompanied by a detailed *curriculum vitae* and the names of three referees, will be received until November 15, 1973, by either Dean Ian E Rusted or Dr B H Sells, Selection Committee, Faculty of Medicine, Memorial University of Newfoundland, St John's, Newfoundland, Canada

(28)

UNIVERSITY OF NEWCASTLE UPON TYNE

THE MEDICAL SCHOOL

TEMPORARY LECTURER IN MICROBIOLOGY

Applications are invited from science graduates with a good honours degree and some experience in microbiology for a whole-time appointment of Temporary Lecturer in the Department of Microbiology Undergraduate courses in microbiology are conducted by the Department for Medical and Dental Students in the Faculty of Medicine, and for Science Students in the Faculty of Science The successful candidate will be encouraged to engage in research, for which there are good facilities The appointment is tenable from October 1, 1973 and will be for one year in the first instance, with a possibility of renewal Commencing salary will be at an appropriate point on the Lecturers (non-medical) salary scale £1,929 to £4,548 per annum Membership of F S S U is required

Further particulars may be obtained from the Registrar, The University, Newcastle upon Tyne NE1 7RU, with whom applications (three copies), together with the names and addresses of three persons to whom reference may be made, should be lodged not later than August 24, 1973 Please quote Reference Na

(67)

FANCY A CHANGE

We have vacancies galore at every grade in the scientific field, including marketing

For further details, write or telephone

WALBROOK APPOINTMENTS,
116 HIGH HOLBORN, LONDON, W C 2
Tel 01-405 8787

(3)

BRISTOL POLYTECHNIC

POST DOCTORAL RESEARCH ASSISTANT

(S R C Award)

A chemist is required to assist in the synthesis of a model for the Haem pocket in Haemoglobin This will involve both heterocyclic and peptide chemistry and will latterly entail the use of vacuum line techniques

The appointment will be for one year only at a salary of £1,788 per annum Opportunities for gaining high level teaching experience are available

Apply by letter, quoting names of two referees and career details, to Dr C L Honeybourne, Department of Science, Bristol Polytechnic, Ashley Down, Bristol BS7 9BU (107)

NATURAL ENVIRONMENT RESEARCH COUNCIL

Institute of Geological Sciences

PALYNOLOGIST SCIENTIFIC OFFICER/ HIGHER SCIENTIFIC OFFICER/ SENIOR SCIENTIFIC OFFICER

A Palynologist with experience of Mesozoic dinoflagellates is required for the Palaeontological Department

The work will be primarily concerned with the Institute's Continental Shelf activities, particularly the investigations into the hydrocarbon fields

The post is at the Northern England Office, Ring Road, Halton, Leeds

QUALIFICATIONS

Scientific Officer minimum requirements normally a degree with 1st or 2nd class honours or equivalent qualification

Higher Scientific Officer and Senior Scientific Officer as above plus at least two years' appropriate postgraduate or other approved experience for H S O and four years' for S S O (Those who expect to complete the specified periods of experience in 1973 may also apply)

AGE

S O normally under 27
H S O normally under 30
S S O normally at least 25 and under 32

SALARIES

Scientific Officer £1,318 to £2,177
Higher Scientific Officer £2 076 to £2,667
Senior Scientific Officer £2,615 to £3,640

Starting salary may be above the minima

The staff of the Council are not Civil Servants, but their pay and conditions of service are similar to those of scientists in the Civil Service

Application forms available from Establishment Office Institute of Geological Sciences, Exhibition Road, London SW7 2DE Please quote SO/PAL/73 Closing date August 17, 1973 (113)

JAMES COOK UNIVERSITY OF NORTH QUEENSLAND

Visit of Vice-Chancellor to United Kingdom

Dr K C Back, Vice-Chancellor of the University will be in London from August 4 to 11 and from August 29 to September 2 and will be available for consultation with any person who may be interested in being considered for the following vacancies which the University has recently advertised

STUDENT COUNSELLOR
LECTURER IN ENGLISH
SENIOR TUTOR IN ZOOLOGY
FOUNDATION CHAIR IN BEHAVIOURAL SCIENCES
LECTURER IN EDUCATION
LECTURER IN GEOGRAPHY
TECHNICAL SERVICES LIBRARIAN
PROFESSOR OF BOTANY
SENIOR LECTURER IN ORGANIC CHEMISTRY

Letters of enquiry should be addressed to him, c/o P B Hetherington, Association of Commonwealth Universities, 36 Gordon Square, London WC1H 0PF (116)

South African Atomic Energy Board

Radiochemist or Radiopharmacist

Applications are invited from suitably qualified and experienced persons to fill a vacancy for a chemist in radioisotope production for the synthesis of radiopharmaceuticals The vacancy exists in the Radioisotope Group of the Chemistry Division

The successful applicant will have to do research on and development of radiopharmaceuticals, such as short-lived generator produced radionuclides, e g technetium-99m, indium-113m, iodine-131, and labelled compounds The minimum qualification is a university degree in organic chemistry or pharmacy, or an appropriate technical diploma Post-graduate research experience will be a recommendation

The salary will be in the range of R4200 to R9300 (£2400 to £5360 approx) per annum plus a pensionable allowance of 15% depending on qualifications and experience Fringe benefits include medical benefit scheme, assisted housing loan scheme, housing subsidy scheme, pension and group insurance scheme, annual leave bonus, ample leave privileges and free transport between Pretoria and the Board's site A person appointed from overseas will receive financial assistance in regard to travelling expenses and the cost of transporting his furniture and effects including a motor car He is required to make use of all assistance given by the South African Department of Immigration, the amount received from the said Department will be deducted from the financial assistance offered by the Board He is also required to serve the Board for two years in consideration of the financial assistance received A non-South African appointee must undertake to apply for South African Citizenship as soon as he qualifies therefore

Written applications, giving full details of qualifications, experience, employer and salary, etc should be addressed to

South African Embassy, Office of the Scientific Counsellor, Chichester House, 278 High Holborn, LONDON WCIV 7HE (telephone 01-242-9641)

(58)

Research and Development with Roussel

Roussel Laboratories Limited, one of the major pharmaceutical companies in the U K require a PHARMACOLOGIST at their new Research and Manufacturing premises in Swindon, Wiltshire

PHARMACOLOGIST

A pharmacologist is required to join a small team researching in the area of C N S

Applicants should have graduate or equivalent qualifications and preferably relevant industrial experience

A progressive salary will be offered and our fringe benefits are excellent

If you are interested, please telephone or write to

Mr D Lawler,
Roussel Laboratories Ltd,
Covingham,
SWINDON
Telephone 0793 24411

ROUSSEL

(104)

Experimental Toxicologist

Tunstall Laboratory, Shell Research Limited

This laboratory which has a multi-disciplinary approach to toxicology wishes to appoint further experimental toxicologists Intending applicants should hold a good degree in medicine, veterinary science, pharmacy or biological subjects

Experience in the use of laboratory animals in safety evaluation is desirable but not essential as relevant training can be given

A progressive career structure will be offered to the successful candidate and there is the possibility of studying for a higher degree

Please apply in writing to Shell Research Limited, Recruitment Division (N), PNEL/31, Shell Centre, London SE1 7NA.

(111)

JUNIOR TECHNICAL OFFICER

The Medical Research Council has a vacancy for a Junior Technical Officer in its Clinical and Population Cytogenetics Unit at the Western General Hospital, Crewe Road, Edinburgh EH4 2XU The successful applicant will form part of a team using long-term cultures of human lymphoid cells for studying mutation induction and other genetic problems

Applicants should possess a good honours degree in a biological science and the initial salary will depend upon age and qualifications Applications stating age, qualifications and experience together with the names of two referees should be sent to the Unit Administrative Officer at the above address by August 18, 1973 (83)

Tissue and Cell Culture

Our Research Department is situated in Nottingham in modern well-equipped laboratories and continues to produce sound achievements in fundamental and applied research There is now an opportunity for a **SENIOR TECHNICIAN** (Grade 7 on a seven point scale) to join a team investigating cellular aspects of rheumatic diseases in the search for new medical products

Applications are invited from candidates possessing at least an H N C or equivalent qualification in a medical or biological science together with experience in mammalian cell and tissue culture techniques Experience in the fields of biochemistry or immunology, though not essential, would be an added advantage

Conditions of employment are first class and include contributory pension and profit earning bonus schemes Some help with relocation expenses will be granted where appropriate

Please write for an application form to

Boots

J F Patison, Employment Services Department,
The Boots Company Ltd,
Station Street, Nottingham, NG2 3AA

(109)

UNIVERSITY OF SHEFFIELD

DEPARTMENT OF HUMAN BIOLOGY AND ANATOMY

SENIOR LECTURER required Applicants must be medically qualified and capable of teaching topographical anatomy and neuroanatomy to medical and dental students Research interests in the central or autonomic nervous systems desirable Excellent research facilities, particularly in the fields of ultrastructure, histochemistry and autoradiography Salary in the range £4,368 to £5,496 with F S S U provision

Applications (8 copies) with the names and addresses of three referees, should be sent to the Registrar and Secretary, The University, Sheffield S10 2TN, by August 20, 1973 Further details may be obtained by writing informally to Professor R Barer Quote Ref R 54/G (9)

READVERTISEMENT

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

APPOINTMENT OF PHYSICIST

A Physicist is required to study interactions between the constituents of milk and cream, subsequent to homogenization, that affect the long-term stability of the product The person appointed would be expected to contribute to the solution of kindred problems encountered in the selective ultrafiltration and concentration of milk and milk products by cold processes

Applicants should have a 1st or Upper 2nd honours degree in physics or in biophysics, or an equivalent qualification Evidence of interest, or preferably postgraduate training, in colloid science, membrane transport or the physics of macromolecules, would be sought

Appointment would be in the grade of Scientific Officer (£1,318 to £2,177) or Higher Scientific Officer (£2,076 to £2,667), depending on age, qualifications and experience Application forms are obtainable from the Secretary, N I R D, Shinfield, Reading RG2 9AT Quote Reference 73/7

Previous applicants should not re-apply (12)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS AL5 2JQ

CHEMIST required to work under senior staff on annual changes in soil nutrients during and after crop growth Interest in growth of crops and experience in scientific monitoring in the field an advantage Minimum qualification pass degree, H N C in Chemistry with Botany subsidiary, or equivalent

Appointment in grade of Scientific Officer, starting salary £1,318 to £1,590 (depending on qualification and experience) on scale to £2,177 Superannuation

Applications, naming two referees and quoting reference 1912, to The Secretary, by August 13, 1973 (16)

ROTHAMSTED EXPERIMENTAL STATION

HERPENDEN, HERTS AL5 2LQ

SCIENTIFIC OFFICER to run assay service in Radiochemistry Laboratory, including maintenance of nucleonic and electrical equipment, under supervision of senior staff Interest in simple computer programming is desirable Minimum qualification pass degree, H N C or equivalent in relevant discipline

Appointment in grade of Scientific Officer (£1,318 to £2 177) or Higher Scientific Officer (£2,076 to £2,667) At least five years' post-qualification experience required for appointment in the higher grade Superannuation

Applications, naming two referees and quoting reference 1922, to The Secretary, by August 13, 1973 (17)

BREWING INDUSTRY RESEARCH FOUNDATION

NUTFIELD, REDHILL, SURREY

ENZYMOLOGIST

A Biochemist is required to purify and study enzymes and other proteins of importance in malting and brewing

Candidates should have a good honours degree in biochemistry or a research degree which required considerable experience in enzymology

The starting salary will depend upon experience, but will fall within the range £1,849 to £2,448 per annum, with a possible extension to £2,848

Applications, together with a curriculum vitae and the names of two referees, should be sent to the Administrative Manager at the above address (38)

UNIVERSITY OF SHEFFIELD

DEPARTMENT OF PURE MATHEMATICS

Applications are invited for the post of JUNIOR RESEARCH FELLOW in the above Department, tenable from October 1, 1973 Salary £1,326 postgraduate or £1,560 postdoctoral a year

Further particulars from the Registrar and Secretary, to whom applications (three copies) should be sent by August 15, 1973 Quote Ref R 59/G (40)

UNIVERSITY OF ZURICH SWITZERLAND

DIVISION OF CANCER RESEARCH

1 **Research Assistantship in Experimental Pathology**

2 **Research Assistantship in Biochemistry—Immunochemistry**

required from October 1, 1973, or as soon after as possible

Applicants will work with experimental models on invasive growth and spread of cancer with emphasis on the role of morphological and physicochemical properties of the cell surface Salary according to Swiss university standards

Knowledge of German not necessary

Applications, with the names of two referees, should be sent to Abteilung für Krebsforschung, Aussenstation der Universitat Zurich, Birchstrasse 95, 8050 Zürich, Switzerland (23)

UNIVERSITY OF ZÜRICH SWITZERLAND

DIVISION OF CANCER RESEARCH

1 **Research Technician in Tissue Culture**

2 **Research Technician in Biochemistry**

required from September 1, 1973, or as soon after as possible

Our team works with experimental models on invasive growth and spread of cancer with emphasis on the role of cell surface properties Work will necessitate experience in fundamental techniques of cell and tissue culture and in standard methods of protein and carbohydrate determinations, respectively

Knowledge of German not essential

Please apply to Abteilung für Krebsforschung, Aussenstation der Universitat Zurich, Birchstrasse 95, 8050 Zurich, Switzerland (24)

AGRICULTURAL RESEARCH COUNCIL

INSTITUTE FOR RESEARCH ON ANIMAL DISEASES

COMPTON, NR NEWBURY, BERKS

HEAD OF DEPARTMENT OF FUNCTIONAL PATHOLOGY

This Senior Principal Scientific Officer vacancy is for a veterinary scientist with wide experience of research into nutritional and metabolic disorders ("production disease") of farm livestock A range of modern equipment is available including auto-analysers, automatic radioisotope counting apparatus and the Compton whole body counter for large animals There are very good facilities for conducting experiments both in the laboratory and on a field scale

Salary will be in the range £5,550 to £6,460, an allowance of 4½ per cent being paid to offset contributions to F S S U

Further particulars may be obtained from the Secretary of the Institute to whom applications should be sent together with the names of two referees not later than August 31, quoting ref 146 (26)

THE GENERAL INFIRMARY AT LEEDS

The Department of Nuclear Medicine has a vacancy for a BASIC GRADE BIOCHEMIST, to work as a member of a team with another Biochemist, Medical Graduates, and Technicians on a research programme investigating thyroid diseases The work will involve radioimmunoassay and related techniques for which training will be provided, if necessary The appointment will be for two years with a possible extension for a third year

Some post-graduate experience would be an advantage but is not essential If it were advantageous to the successful applicant he would be encouraged to apply to the University for registration as an M Phil student under the supervision of the University Department of Chemical Pathology

Salary will be scale £1,566 to £1,980 or £1,278 to £1,980, depending on qualifications The post-probationary scale would apply to suitably qualified applicants who are working in the National Health Service at the moment

Further information and an application form may be obtained from Dr Clive Hayter, Consultant in Nuclear Medicine, the General Infirmary, Great George Street, Leeds LS1 3EX (27)

UNIVERSITY OF LONDON CHAIR OF RADIOTHERAPY AT INSTITUTE OF CANCER RESEARCH

The Senate invite applications for the above Chair tenable at the Institute of Cancer Research in association with the Royal Marsden Hospital The appointment will carry an honorary consultancy in Radiotherapy at that Hospital

Applications (10 copies) must be received not later than Friday, September 14, by the Academic Registrar (N), University of London, Senate House London WC1E 7HU, from whom further particulars may be obtained (33)

Carreras Rothmans

SECTION MANAGER

Biology/£3000+

We seek a scientist with drive and creativity to lead an experienced team of scientists and technologists at the Research Division Laboratories located at Basildon in Essex The current work programme includes the development of in-vitro bioassay techniques and the Section Manager is expected to contribute to the planning of the future programme and to undertake its implementation

Candidates, preferably between 26 and 35 years, should have at least a good honours degree in biology, and preferably should have specialized in toxicology, physiology or biochemistry Some industrial experience or the equivalent, not necessarily in the tobacco industry, including the leadership of research teams is essential This is a senior appointment and the successful applicant will report directly to the Research Manager

There are generous pension, life assurance and other fringe benefits

Applications giving brief details of qualifications and experience should be sent to

Personnel Manager,
CARRERAS ROTHMANS LIMITED,
Christopher Martin Road, Basildon, Essex.

(117)

Wellcome

Interferon Studies

The Scientist who undertakes the interferon studies will work in the Department of Virology (Head, Dr N B Finter), but in association with Dr K H Fantes (Department of Biological Chemistry)

Candidates should have had appropriate training in microbiology and preferably some post-doctoral experience in virology with evidence of research ability Familiarity with interferon techniques would be advantageous, but is not essential as training can be given The appointment would, in the first instance, be for three years

Applications, giving brief details of age, qualifications and experience should be sent to the **Personnel Manager,**
THE WELLCOME RESEARCH LABORATORIES,
Langley Court, Beckenham, Kent.

(69)

Medical Administration Assistant

We have a vacancy in our Scientific Information Department for a young graduate in a biological science

The work will include scientific report writing, organisation of material for submission to the Committee on Safety of Medicines and assistance with budgetary control of medical projects

Essential attributes are an aptitude for writing clear and concise English and the ability to organise complex material as well as administrative flair Previous experience in the Pharmaceutical industry would be an advantage

Please apply to
Personnel Officer, John Wyeth & Brother Limited,
Huntercombe Lane South, Taplow, Maidenhead, Berks
Telephone Slough 28311

Wyeth

(77)

Tropical Products Institute, London

Information scientist

£2790—£3815

in the Information Department to take charge of the Technical Index which provides a unique guide to the literature on tropical agriculture and to the technology and marketing of tropical products

Current duties include selecting, evaluating and indexing information from a wide range of scientific and technical publications, maintaining an effective retrieval system, and assisting with the training of overseas personnel Later, the successful candidate will most probably participate in planning and introducing computerized retrieval procedures in co-operation with international information agencies

Candidates (preferably aged 35–45) must have knowledge of the latest indexing/abstracting techniques and an awareness of current developments in the agricultural information field They should normally have a degree, HND, HNC or equivalent qualification in an appropriate subject—e g combination of chemistry and biology (especially botany)—but applicants lacking formal qualifications and having particularly relevant experience may be considered Working knowledge of a foreign language desirable

STARTING SALARY will be within the quoted scale Non-contributory pension scheme

For full details and application form (to be returned by 29 August 1973) write to Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB or telephone BASINGSTOKE 29222 ext 500 or LONDON 01-839 1992 (24 hour answering service) Please quote S/8339.

(31)

UNIVERSITY OF NEW SOUTH WALES

SCHOOL OF MICROBIOLOGY

PROFESSOR

Applications are invited for appointment to the Chair, which will become vacant early in 1974 on the retirement of Professor J M Vincent The Professor will supervise and participate in those areas of teaching and examining undergraduate and postgraduate students in the School which can be broadly categorized as non-medical, and will engage in and promote research and advanced study in the field of his chair Salary $A19,102 per annum Subject to the consent of the University Council, Professors may undertake a limited amount of higher consultative work The University reserves the right to fill any Chair by invitation

Details of appointment, including superannuation study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square London WC1H 0PF (Tel 01-387 8572)

Applications close in Australia and London on **September 28, 1973** (65)

SUNDERLAND POLYTECHNIC

SCHOOL OF PHARMACY

PRINCIPAL LECTURER IN PHARMACOLOGY

£3,581 to £3,989 extended to £4,499

Applicants should have a postgraduate qualification in an appropriate field and experience of conducting and supervising research in Pharmacology and/or related subjects Experience in teaching would be an advantage

An application form and further particulars may be obtained from the Personnel Officer, Sunderland Polytechnic, Chester Road, Sunderland SR1 3SD This should be returned not later than August 18, 1973 (34)

The Hatfield Polytechnic

Department of Biological Sciences

RESEARCH FELLOW

required to commence September to work, preferably at postgraduate level, on Biochemical and Physiological problems associated with the transfer of Tissue Culture Plantlets, to Inert Supporting Media

The appointment will be initially for two years

Starting salary would be within L1 scale £1,660 to £2 847 (x85)

Further details and application forms may be obtained from the Staffing Officer, The Hatfield Polytechnic, P O Box 109, Hatfield, Herts AL10 9AB Completed applications should be returned by August 15

Please quote ref 331/N (35)

THE UNITED CAMBRIDGE HOSPITALS

Research post suitable for a qualified Technician or experienced graduate exists in the Department of Haematology, Addenbrooke's Hospital, Hills Road, Cambridge Experience in tissue culture an advantage Excellent working conditions in a new laboratory complex

Enquiries to Mr D W Finch, Cambridge 45151 ext 7133, applications to the Personnel Officer (36)

SENIOR FACULTY IN MEDICINAL CHEMistry An experienced individual with an active research program publications and teaching experience in synthetic organic chemistry is being sought to head an academic Division of medicinal Chemistry with the Division of Pharmacological Sciences Teaching responsibilities will include graduate instruction in medicinal chemistry, chemical biology and pharmacology The Health Sciences Center is an equal opportunity employer and applications from members of minority groups or women are welcome—Address reply to Dr Arthur Upton, Dean, School of Basic Health Sciences, SUNY at Stony Brook, Stony Brook, New York 11790 (37)

UNIVERSITY OF OXFORD

LABORATORY OF MOLECULAR BIOPHYSICS

POSTDOCTORAL RESEARCH ASSISTANTSHIP IN PROTEIN CRYSTALLOGRAPHY

Applications are invited for a Postdoctoral Research Assistantship to work on the crystal structure of phosphorylase b The research will involve the development of efficient methods of data collection for large biological molecules with reference to the high resolution structure determination of phosphorylase

The appointment is for a period of three years with a salary starting at £1,764 Previous research experience in crystallography is essential

Applications, including a brief curriculum vitae, research experience, and names and addresses of two referees, should be sent to Dr L N Johnson, Laboratory of Molecular Biophysics, Zoology Department, South Parks Road, Oxford, as soon as possible (46)

EDITORIAL ASSISTANT

required for metallurgical publications Must have experience in editing technical manuscripts, correcting printers' proofs, etc Salary around £2,000 per annum

Applications in writing to the Editor, Institute of Metals, 17 Belgrave Square, London SW1X 8PU •(47)

MAX-PLANCK INSTITUT FÜR MOLEKULARE GENETIK

WEST BERLIN

RESEARCH ASSISTANT

required for studies on the three-dimensional structure of bacterial ribosomes Applicants should hold a degree or H N C in chemistry or biochemistry (or equivalent qualification), and should have an interest in protein synthesis and the chemistry of proteins and nucleic acids The appointment is vacant from October 1, and salary will be in the region of 17,000 DM per annum (ca £2,500) depending on age and qualifications

Applications should be made before August 31 to Dr Richard Brimacombe, National Institute for Medical Research, Mill Hill, London NW7 1AA (01-959 3666, Ext 268), from whom further details may be obtained (45)

MIDDLESEX HOSPITAL MEDICAL SCHOOL

COURTAULD INSTITUTE OF BIOCHEMISTRY

RESEARCH ASSISTANT

A vacancy exists for a recent graduate with a good degree in biochemistry to study lipoprotein biosynthesis and metabolism, with special reference to heart disease The post carries a salary of up to £1,227 per annum

Applications, including a curriculum vitae and the names and addresses of two referees, to Dr G L Mills (N), Courtauld Institute of Biochemistry, The Middlesex Hospital Medical School, London W1P 7PN (57)

UNIVERSITY OF SURREY

Department of Mechanical Engineering

RESEARCH FELLOW

(with experience in electronics)

A Research Fellow is required to work on an experimental investigation of the turbulence structure of jets A principal aim of the project would be to develop a technique for tracking the interface between the turbulent and non-turbulent fluid and this would involve developing some interesting optical and electronic systems

The appointment would be initially for two years with the possibility of a further extension if the project is developing in a satisfactory way The salary would be in the range from £2,000 to £2,500 per annum, depending on experience

Applicants should send details of their career and qualifications with the names and addresses of two referees to Dr L J S Bradbury, Department of Mechanical Engineering, University of Surrey, Guildford Surrey GU2 5XH (119)

BIRKBECK COLLEGE

(UNIVERSITY OF LONDON)

Applications are invited for the post of ADMINISTRATIVE ASSISTANT Salary scale £1 929 to £2,058 by £165 to £3,048, plus London Allowance of £162 per annum

Further particulars and forms of application should be obtained from the Secretary (N), Birkbeck College, Malet Street, London WC1E 7HX Closing date August 31 (125)

DEPARTMENT OF MICROBIOLOGY

GUY'S HOSPITAL MEDICAL SCHOOL

RESEARCH ASSISTANT

required for one year in the first instance in a team studying Viral Transformation in Relation to Membrane Changes and Regulation of Cell Growth Some postdoctoral experience in virology or membrane biology desirable Salary up to £2,388 according to experience, plus London allowance and superannuation

Applications, with curriculum vitae and names of two referees, should reach the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, by August 31. (64)

UNIVERSITY OF ZAMBIA

Applications are invited for post of (a) CHIEF TECHNICIAN or (b) SENIOR TECHNICIAN IN DEPARTMENT OF GEOGRAPHY Appointee will be expected to take administrative charge of all technical services in geography under the general direction of the Head of the subject, to act as cartographer and principal draughtsman, and to instruct young Zambian assistants in draughtsmanship Relevant experience in a university geography department is essential and some practical knowledge of photography and of instruments commonly used in geography would be an added recommendation Salary scales (a) K3,300 to K4,900 per annum, (b) K2 900 to K3,500 per annum (£1 sterling= K1 65) Family passages various allowances, biennial overseas leave, children's education allowances and holiday visit passages, superannuation and medical aid schemes

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail not later than August 29, 1973, to the Registrar, University of Zambia, P O Box 2379, Lusaka, Zambia Applicants resident in U K should also send one copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT Further particulars may be obtained from either address (49)

VACANCY OF RESEARCH UNITS OF "L'INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE"

The Direction of a Research Unit in Fundamental or Applied Virology, located in Lyon (France), and the Direction of a Research Unit in Psychology of Childhood, located in Montpellier (France), will be vacant on January 1, 1974

Candidates of any nationality can apply

Application forms can be obtained from

Institut National de la Santé et de la Recherche Medicale,
3 Rue Léon Bonnat,
75782 Paris Cédex 16
c/o Madame Laurent

Date limit for the Unit of Fundamental or Applied Virology is October 31, 1973, and for the Unit of Psychology of Childhood is November 30, 1973 (62)

UNIVERSITY OF READING

RESEARCH ASSISTANTS

(2 vacancies) required to work on the evaluation of Skylark rocket photography of Argentina for a period of one year from October 1, 1973 One Assistant will work in the Department of Geography at Reading on crop and land use identification Degree in botany, geography, or earth science required, experience in air photo interpretation desirable The other Assistant will work in the Department of Physics, Bedford College, University of London, on automated analysis of photography using computer techniques Degree in physics or mathematics, with a knowledge of computer programming required Salary for these posts £1,500 per annum approximately

Apply, quoting Ref MN51, with full details and the names of two referees, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH (60)

POSITIONS OPEN

THE UNIVERSITY OF CHICAGO

DEPARTMENT OF ANTHROPOLOGY

seeks for possible appointment at any level, candidates for creative research and imaginative teaching in physical anthropology (human evolution, human biology, biological bases of behaviour comparative primate studies, other) Since its charter, the principle of the University has been to appoint without regard to race, religion, sex, or national origin Candidates desiring consideration should send vita and documents demonstrating distinction or potential for distinction to Chairman, 1126 East 59th Street, Chicago, IL 60637 (78)

THE MACAULAY INSTITUTE FOR SOIL RESEARCH

DEPARTMENT OF SOIL FERTILITY

Applications are invited for a SCIENTIFIC OFFICER to study physical characteristics of soils in relation to crop growth Candidates should have a First or Upper Second Class Honours Degree with advanced training in Physics and Mathematics, and preferably some research experience

The appointment will be in the Scientific Officer (£1,590 to £2,177 per annum) or Higher Scientific Officer (£2,076 to £2,667 per annum) grade, according to qualifications and experience, with prospect of promotion to a higher grade Superannuation under F S S U for which a non-pensionable allowance of 4½ per cent is added to salary to offset contributions

Forms of application may be obtained from the Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen AB9 2QJ, to whom they should be returned before August 24, 1973 (Quote Ref 73/15) (91)

UNIVERSITY OF DAR ES SALAAM TANZANIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN PLANT TAXONOMY IN DEPARTMENT OF BOTANY Applicants should have a higher degree, preferably a PhD in Plant Taxonomy plus at least 4 years experience in the field They should also be conversant with the taxonomy of tropical plants Knowledge of modern approaches to taxonomy will be an advantage Appointee will have the following duties organization and teaching of Plant Taxonomy to undergraduates, teaching some undergraduate and postgraduate courses other than taxonomy, establishment of postgraduate courses in taxonomy, research in some taxonomic aspects of certain Tanzanian plants to assist in the running of the Departmental Herbarium in co-operation with the Herbarium staff Salary scales (a) T£2,380 to T£2,800 per annum (b) T£1,898 to T£2,318 per annum (T£1=£1 10 sterling) The British Government may supplement salary in range £550 to £950 per annum (sterling) for married appointee or £300 to £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages F S S U Family passages, biennial overseas leave

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than August 30, 1973, to the Chief Academic Officer, University of Dar es Salaam P O Box 35091, Dar as Salaam, Tanzania Applicants resident in U K should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road London W1P 0DT Further particulars may be obtained from either address (75)

UNIVERSITY COLLEGE, DUBLIN

RESEARCH ASSISTANTSHIP IN QUANTITATIVE GENETICS OF SHEEP GROWTH

Applications for the above post which is supported by a grant from An Foras Taluntais, in the Agricultural Biology Department in University College, Dublin, are invited from graduates having a knowledge of quantitative genetics and/or animal breeding

Salary in the region of £1,200, appointment initially for one year, starting October, 1973

Details are obtainable on request from Dr J C McCarthy of the Agricultural Biology Department, at Ballymun Road, Glasnevin, Dublin 9 (79)

UNIVERSITY COLLEGE OF WALES

WELSH PLANT BREEDING STATION

ELECTRON MICROSCOPY

Applications are invited for a post as ELECTRON MICROSCOPIST on the staff of the Station

The post is concerned with the preparation/examination of material including the production of ultra-thin sections for examination, microscope routines, and also for the routine techniques involved in the serological typing of viruses and bacteria

Candidates should hold a University Pass Degree or National Certificate in an appropriate field

Salary scales

Scientific Officer—£1,318, rising to £2,177 maximum per annum

Higher Scientific Officer—£2,076, rising to £2 667 maximum per annum

The starting point will be determined in relation to the successful candidate's qualifications and experience The post is superannuated

Letters of application, together with the names of two referees, should be sent to the Secretary, Welsh Plant Breeding Station, Plas Gogerddan, Nr Aberystwyth SY23 3EB, on or before August 31 1973 (97)

UNIVERSITY OF DAR ES SALAAM TANZANIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN STATISTICS Candidates should have at least a Master's degree or equivalent Appointee will be expected to teach statistics to undergraduate students He will also be expected to undertake research in his teaching field Salary scales (a) T£2,380 to T£2,800 per annum, (b) T£1,898 to T£2,318 per annum (T£1=£1 10 sterling) The British Government may supplement salary in range £550 to £950 per annum (sterling) for married appointee or £300 to £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visits passages F S S U Family passages, biennial overseas leave

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees should be forwarded by air mail, not later than August 31, 1973, to the Chief Academic Officer, University of Dar es Salaam, P O Box 35091, Dar es Salaam, Tanzania Applicants resident in U K should also forward 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT Further particulars may be obtained from either address (98)

L'ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE

met au concours le poste de

Professeur de Physique Experimentale

Activité de recherche:

participation aux travaux du laboratoire de physique expérimentale plus particulièrement du point de vue théorique Le domaine actuel de recherche du laboratoire est l'éude de l'effet de taille (quantique, optique et thermodynamique)

Activité d'enseignment:

Un cours de physique générale au niveau du premier cycle donné à l'une des sections d'ingénieurs de l'école polytechnique Participation éventuelle à un cours plus spécialisé au niveau du deuxième cycle

Sont invités à soumettre leur candidature les physiciens, de nationalité suisse ou étrangère, au bénéfice d'un titre de docteur, possedant une bonne formation en physique expérimentale mais ayant, si possible, actuellement une activité en physique théorique

Les personnes interessées à faire acte de candidature voudront bien demander le dossier relatif à ce poste à la

Direction de l'Ecole polytechnique féderale de Lausanne, 33 av de Cour, CH-1007 Lausanne-Suisse (25)

THE MACAULAY INSTITUTE FOR SOIL RESEARCH

DEPARTMENT OF SOIL FERTILITY

Applications are invited for a SCIENTIFIC OFFICER to assist in laboratory and field measurements of physical properties of soils in relation to crop growth Candidates should have a Pass Degree or Higher National Certificate in Physics some knowledge of Mathematics, Chemistry and or Soil Science an advantage

The appointment will be in the Scientific Officer grade, starting salary within the range £1,318 to £2,177 per annum, according to qualifications and experience, with prospect of promotion to a higher grade Superannuation for which a non-pensionable allowance of 5½ per cent is added to salary to offset contributions

Forms of application may be obtained from the Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen AB9 2QJ, to whom they should be returned before August 24, 1973 (Quote Ref 73/14) (92)

PRE DOCTORAL BIOCHEMIST

required to work in the Department of Chemical Pathology on an active Endocrinological Research Programme Experience in Radioimmunoassays an advantage, but not essential Salary according to the Whitley Council scales

Applications in writing to Profesor J R Hobbs, Department of Chemical Pathology, Westminster Medical School, 17 Page Street, London, S W 1 (96)

ROYAL POSTGRADUATE MEDICAL SCHOOL

SENIOR TECHNICIAN required in Department of Medicine The appointee will assist in a research programme concerned with the detection of early bronchial disease by sensitive physiological tests Qualifications H N C in physiological measurement of equivalent Salary in range £1,473 to £2,169 per annum, according to qualifications and experience

Applications by August 13, to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 2/213/N (76)

MEDICAL RESEARCH COUNCIL BLOOD Group Unit, Lister Institute, Chelsea Bridge Road, London SW1W 8RH Graduate needed in October preferably with some immunological or genetical education Please apply in writing (94)

University of Bradford

LECTURESHIP IN BIOCHEMISTRY

Applications are invited for the post of LECTURER in BIOCHEMISTRY Candidates are expected to have a good honours degree and to have appropriate research experience Salary within scale £1,929 to £4,548 per annum Superannuable (F S S U)

Further particulars and application forms (returnable as soon as possible) from the Registrar, Post ref B/L/11/X, University of Bradford, Yorkshire BD7 1DP (81)

ROYAL POSTGRADUATE MEDICAL SCHOOL

TECHNICAL OFFICER (Graduate Chemist/Biochemist/Pharmacist) required to join group studying drug metabolism in animals and man Duties involve the supervision and development of gas chromatographic assay methods for drugs and metabolites in biological fluids Salary according to qualifications and experience

Applications to the Secretary (N), Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 20/279 (74)

UNIVERSITY OF HULL

DEPARTMENT OF BIOCHEMISTRY

POSTDOCTORAL RESEARCH ASSOCIATE

A vacancy exists for a biochemist or microbiologist to join a small team under the direction of Dr Colin Ratledge investigating aspects of hydrocarbon utilization coupled with lipid biosynthesis in yeasts The successful candidate should have or expect to obtain a Ph D before taking up the appointment which is due to start October 1, 1973 Technical assistance will be available

Appointment for up to three years Funds provided by S R C

Salary Scale £1,887 £2,010 £2,079 (under review) plus F S S U

Further details may be obtained from The Registrar, The University Hull HU6 7RX, Yorkshire, to whom applications with the names and addresses of two referees should be submitted as soon as possible, but certainly not later than September 3, 1973 (89)

SOUTHMEAD HOSPITAL, BRISTOL

A SCIENTIFIC OFFICER

is required to work in the Department of Medical Microbiology An Honours degree in Microbiology, or an Honours degree in a related subject with appropriate postgraduate experience is needed The appointee will work in the routine diagnostic laboratory but will also be encouraged to participate in research particularly in the field of antibiotic assay An interest in statistics and computing would be an advantage

The Hospital is associated with the University of Bristol in medical undergraduate teaching The Department performs routine and more specialised investigations for the hospital Facilities exist for registering a higher degree

Application forms should be obtained from the Group Secretary, Southmead Hospital, Bristol BS10 5NB and returned by August 17 1973

For further details or arrangements to visit the laboratory, contact Dr D S Reeves, in the Department (86)

UNIVERSITY OF WALES

BOARD OF CELTIC STUDIES

Applications are invited for the post of RESEARCH ASSISTANT in ARCHAEOLOGY The assistant will be responsible for conducting a programme of scientific analysis of Prehistoric Bronze Implements from Wales and should possess a good Honours degree (or postgraduate qualifications) in Applied Physics or Materials Science Salary £1,764 to £2,079 (scale under review)

Further particulars can be obtained from the Registrar, University Registry, Cathays Park, Cardiff, with whom applications should be lodged not later than August 15, 1973 (93)

The Macaulay Institute for Soil Research

Head of Department Soil Organic Chemist

Applications are invited for this vacancy The appointment will be at the Senior Principal Scientific Officer level

It is proposed that the successful applicant should lead work on soil organic matter (other than pedological investigations on peat and forest soils), on soil and plant biochemistry, and on some aspects of plant physiology, and collaborate closely with colleagues engaged on soil microbiology and in other areas of scientific work of the Institute

An organic chemist with an interest in soil problems and some knowledge of microbiological chemistry would be most appropriate The person appointed would be expected to undertake some reorientation of the present departmental programme

A high level of scientific attainment, and the capacity to direct and guide the work of others, together with a readiness to engage in collaborative projects would be required

The salary scale of the Senior Principal Scientific Officer grade is £5,550-£6,460 per annum, plus a non-pensionable allowance of 4¼ per cent to offset F S S U superannuation contributions

Forms of application may be obtained from the **Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen AB9 2QJ,** to whom they should be returned by September 17, 1973

Quote Ref 73/18 (133)

UNIVERSITY OF ASTON IN BIRMINGHAM

Department of Geological Sciences

BACTERIOLOGIST

A research student is required to investigate the potential of using bacteria in mining sulphide ores Proficiency in experimental bacteriological technique is essential but no knowledge of geology is required The applicant will register for an M Phil degree Research Studentship available

Applications to Professor D D Hawkes Head of Department of Geological Sciences The University of Aston in Birmingham Gosta Green, Birmingham B4 7ET (108)

MASSEY UNIVERSITY

PALMERSTON NORTH NEW ZEALAND

POSTDOCTORAL RESEARCH FELLOW

DEPARTMENT OF SOIL SCIENCE

Applications are invited for the position of Post-Doctoral Research Felow in the Department of Soil Science The appointee will work with Professor J K Syers on a project concerning the removal of phosphate from waters and effluents by clay minerals and hydrous metal oxides

Applicants shoud have a good B Sc (Hons) degree and have completed or are about to complete a Ph D degree in Chemistry, Soil Science or Civil/Chemical Engineering

The position is for one year and the salary is $NZ5,000 per annum The successful applicant will commence duties at a mutually convenient time, preferably before January 1 1974

Further information concerning the research project and the University together with conditions of appointment may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572), or from the Registrar of the University

Applications close on September 7, 1973 (99)

AREA LABORATORY KING EDWARD VII HOSPITAL WINDSOR

DEPARTMENT OF MICROBIOLOGY

Applications are invited immediately for the following posts

(1) SENIOR TECHNICIAN

(2) TECHNICIAN

(3) JUNIOR TECHNICIANS

The Department provides a comprehensive service in Microbiology for approximately 1 000 beds and for Out-patient Clinics and General Practitioners in the area Expansion of the Hospital Services is anticipated in the near future The Hospital is situated close to public termini within easy access of London by road and has its own swimming pool

Applications to the Senior Pathologist, Area Laboratory Tel Windsor 61424 (enquiries to Senior Chief Technician) (102)

UNIVERSITY OF SUSSEX

SCHOOL OF BIOLOGICAL SCIENCES

RESEARCH ASSISTANT

Applications are invited from graduates, preferably in physiology or biology, for a post of Research Assistant to collaborate in a programme of research into the mechanisms involved in regulating the uptake and exchange of ions including calcium by the snail hosts of schistosomiasis

Salary on the scale £1,002 to £1,362 per annum

Application forms can be obtained from the Secretary of Science Science Office (Establishment) the University of Sussex Falmer, Brighton BN1 9RH (103)

GLASSHOUSE CROPS RESEARCH INSTITUTE

FLORICULTURE RESEARCH

Applications are invited for new post in Horticulture Department aimed to strengthen applied research in floriculture Candidates should have a horticultural or applied botanical background with degree or National Diploma in Horticulture or degree in Botany or Biology Appointment within grade of S O or H S O depending on qualifications and experience Salary £1,318 to £2,177 (S O), £2,076 to £2 667 (H S O) plus 5½ per cent to offset superannuation contributions Minimum 5 years' post-qualifying experience for appointment in higher grade

Further particulars from Secretary of the Institute, Worthing Road, Rustington Littlehampton, Sussex, to whom application should be sent before August 31 1973 (88)

UNIVERSITY OF NOTTINGHAM

CANCER RESEARCH CAMPAIGN LABORATORIES

Applications are invited for postgraduate and post-doctorate appointments sponsored by the Cancer Research Campaign to work on the biochemistry of tumour associated antigens under the direction of Professor R W Baldwin Applicants should have appropriate experience in biochemistry and training in immunology, although desirable is not essential

The postdoctorate appointment (job ref 292) will be on a salary scale £1 929 £2,058, £2,223 per annum plus F S S U

The postgraduate appointment (job ref 292) will be on a salary scale £1,422, £1,494 £1,569 per annum and there will be an opportunity to read for a higher degree

Further particulars and forms of application—returnable not later than August 20 1973—from the Staff Appointments Officer, University of Nottingham, University Park Nottingham NG7 2RD (120)

THE HATFIELD POLYTECHNIC

Temporary Lecturer (Grade I) in Biochemistry

A biochemist with interests in the general area of mammalian biochemistry/biochemical pharmacology is required to assist with the teaching of biochemistry to honours degree level The appointment will be for one year, and the successful candidate will be expected to have appropriate research experience and to commence duties at the end of September if possible

Salary £1 660 to £2,685 per annum

Specific enquiries may be made to Head of Biochemistry Group, Department of Biological Sciences, The Hatfield Polytechnic

Further information and application forms may be obtained from The Staffing Officer, The Hatfield Polytechnic P O Box 109, Hatfield Herts AL10 9AB Completed application forms must be returned by August 31, 1973 Please quote ref 340/N (123)

TECHNICAL OFFICER

preferably with degree in biology or chemistry required at M R C Rheumatism Unit, Canadian Red Cross Memorial Hospital, Taplow, Maidenhead, Berkshire, for research on immunological and experimental aspects of rheumatic diseases

Post vacant October 1, 1973

Applications, with names of two referees, to the Director (101)

FELLOWSHIPS AND STUDENTSHIPS

UNIVERSITY OF GLASGOW

DEPARTMENT OF ELECTRONICS AND ELECTRICAL ENGINEERING

RESEARCH STUDENTSHIPS

A number of research studentships are available in this Department for research into the physical properties of polymer melts and liquids The research work envisaged is of an interdisciplinary nature and will be carried out in a well-established Research Group forming part of the Glasgow Polymer Centre

An S R C (CASE) studentship is also available for an experimental and theoretical study of the incendivity of discharges from electrostatically charged non-conducting media This work is to be done in collaboration with I C I (Organics Division)

Honours graduates and students expecting to graduate this year in Physics Chemistry, Materials Science or Electronics and Electrical Engineering are invited to apply for these posts Conditions of award and duration of the studentships are subject to the usual S R C requirements and it is expected that the research student will register for a higher degree for which fees are paid

Applications, together with the name of one referee should be sent as soon as possible to Professor J Lamb, Department of Electronics and Electrical Engineering, The University of Glasgow Glasgow G12 8QQ In reply please quote Ref No 3331 (84)

JOHN INNES INSTITUTE

RESEARCH STUDENTSHIP

Applications are invited from first or upper second class honours graduates for an A R C Research Studentship in the Department of Ultrastructural Studies at the above Institute The successful candidate will study ultrastructural aspects of plant cell differentiation and its experimental control

The Studentship will be for a period of three years commencing October 1, 1973

Applications should be addressed as soon as possible to the Secretary, John Innes Institute, Colney Lane, Norwich NOR 70F, giving full particulars and the names of two referees (44)

THE QUEEN'S UNIVERSITY OF BELFAST

RICHARDSONS ULSTER STUDENTSHIP

Open to graduates in Agricultural Chemistry, Biochemistry or Chemistry with suitable subsidiary subjects, preference being given to applicants of Northern Ireland parentage The holder will undertake research work connected with plant nutrition or the biochemistry of plant growth and may register for a higher degree of the University The work will be carried out in the Agricultural and Food Chemistry Department of the University

The Studentship is tenable up to three years and its value will be £600 in the first year of tenure rising annually by £50 to a maximum of £700 An allowance of up to £150 per annum will be available for approved expenses

Candidates should apply in writing, giving full details of their qualifications, to the Dean of the Faculty of Agriculture and Food Science, Queen's University, Belfast BT9 5PX, by August 24, 1973 (21)

UNIVERSITY OF MANCHESTER INSTITUTE OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF CHEMISTRY

Applications are invited for the following research appointments tenable in the Department of CHEMISTRY

(i) Postdoctoral Fellowship (S R C) in physical chemistry The project involves the study of dynamical processes in liquids and related systems using Rayleigh light scattering and photon pulse correlation spectroscopy Applicants should have an appropriate theoretical or practical background derived from chemistry, physics or a related subject The appointment will be for up to two years—starting salary in a range up to £1 935 per annum, plus F S S U

(ii) Research Assistantship for work on the chemisorption of chlorine and its effect on thermal decomposition of alkyl halides Applicants should have research experience in catalysis or gas kinetics Starting salary £1,576 per annum, plus F S S U

(iii) A C A P S Research Studentship in the study of kinetics of hydrocarbon oxidation at the high temperatures encountered in flames using mass spectrometric techniques Applicants should have a good honours degree or equivalent

Applications (no forms), comprising a curriculum vitae and particulars of two referees should be addressed to Professor P G Ashmore Department of Chemistry, U M I S T, Manchester M60 1QD as soon as possible (14)

KING'S COLLEGE, CAMBRIDGE

Fellowships in Applied Probability Theory in Relation to Population Biology

Applications are invited for Fellowships in the above field, including population and human genetics, ecology, evolutionary theory, demography and stochastic diffusion processes, to be held (from October 1974, or by arrangement) in the King's College Research Centre where computing facilities are available Senior (age limit of 32 years) and Junior (age limit of 28 years and not more than about 3 years research experience) fellowships are available, together with an unrestricted fellowship which could be held by a senior worker on sabbatical leave Maximum tenure, 4 years Closing dates October 1, 1973 for senior and open November 15, 1973 for juniors Details of stipend, accommodation research facilities, etc from The Convener, King's College Research Centre, King's College, Cambridge CB2 1ST, England (18)

UNIVERSITY OF KEELE

Applications are invited for a RESEARCH STUDENTSHIP in the Department of Chemistry for the chemical investigation of volatile pheromones in insects, leading to an M Sc or Ph D degree The Studentship is funded by the S R C through a Co-operative Award in Science and Engineering, jointly with Rothamsted Experimental Station Harpenden, Herts Candidates with a joint degree in chemistry and biology or chemistry with some biology will be preferred Otherwise normal conditions of eligibility and stipend for S R C Studentships apply

Further information and application forms from Dr E D Morgan, Department of Chemistry, The University, Keele, Staffs ST5 5BG (55)

THE QUEEN'S UNIVERSITY OF BELFAST

SEED POTATO MARKETING BOARD STUDENTSHIP

Applications are invited for the Seed Potato Marketing Board for Northern Ireland Studentship from graduates in Agriculture, Agricultural Science or Science The holder will work in the Department of Mycology and Plant Pathology in the Faculty of Agriculture and Food Science of the University, on potato-tuber diseases and shall be required to study for a higher degree at the University The value of the Studentship, which is tenable for three years, is £675 per annum in addition, up to £135 per annum will be available for University fees and other authorized expenses

Candidates should apply in writing, giving full details of their qualifications, to the Dean, Faculty of Agriculture and Food Science, The Queen's University, Newforge Lane, Belfast BT9 5PX, by August 24, 1973 (20)

CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE

WILMSLOW ROAD, MANCHESTER M20 9BX

Ph D STUDENTSHIPS

Two positions are available (October 1973) in the field of Cell Kinetics (Haemopoietic and Epithelial tissues)

Candidates should have an Upper Second or First Honours Degree and an interest in the subjects

Apply

Professor L G Lajtha,
Paterson Laboratories
Christie Hospital,
Manchester M20 9BX (19)

THE POLYTECHNIC OF CENTRAL LONDON

PCL RESEARCH STUDENTSHIP

£1,320 to £1,485

in the Department of Physics tenable for three years from October 1973 The successful candidate will investigate the Track Structure of Ionising Radiation using a Low Pressure Cloud Chamber The work will be carried out in the Health Physics and Medical Division at Harwell and the student will be expected to register for the degree of PhD (C N A A) Applicants should be honours graduates (or expect to graduate this summer)

Details and application form from The Establishment Officer, 309 Regent Street, London W1R 8AL Closing date, August 16, 1973 Please quote reference 826 (82)

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20124 MILANO, Italy. (2)

UNIVERSITY OF WALES
University College of Swansea

Post-Doctoral Fellowships

Applications are invited for two vacancies of postdoctoral fellow in the Department of Chemistry to work on

(a) applications of carbohydrate N-nitrosoamides, and
(b) synthesis of branched-chain sugars and aldulose derivatives

Both posts are tenable from October 1, 1973 and will be for one year, at a salary of £1,929 per annum

Application forms should be returned as soon as possible

Department of Chemistry

Applications are invited for vacancies of Research Demonstrator in the Department of Chemistry Applicants in all branches of Chemistry will be considered but candidates should hold, or expect to receive a Ph D Degree in the near future Those appointed will be expected to participate in one of the numerous research programmes in the department

The posts, which are tenable from October 1, 1973, will be for one year in the first instance The salary will be on the scale £1,584 to £1,665 per annum together with F S S U benefits

The closing date is **Friday, August 31, 1973.**

Further particulars and application forms for both of the above may be obtained from the Registrar/Secretary, University College of Swansea, Singleton Park, Swansea SA2 8PP, to whom they should be returned by the specified dates

(53)

UNIVERSITY OF STRATHCLYDE

Department of Metallurgy

RESEARCH FELLOWSHIP

Thermodynamics and Electronic Structure of Alloys

Applications are invited for a Research Fellowship, tenable for two years in the first instance, from candidates with interests in MATERIALS PHYSICS and/or THERMODYNAMICS of ALLOYS The salary will be between £1,923 and £2,079 (under review) with F S S U benefits, placing according to qualifications and experience

The successful applicant will work with an established group, supported by the Science Research Council, in the field of THERMODYNAMICS AND ELECTRONIC STRUCTURE OF METALS AND ALLOYS studied by MASS SPECTROMETRY, X-RAY PHOTOELECTRON SPECTROSCOPY and SOFT X-RAY SPECTROSCOPY A PhD in Metallurgy, Physics or Chemistry, and relevant research experience is desirable

RESEARCH STUDENTSHIP

Thermodynamics and Electronic Structure of Alloys

Applications are invited for an SRC Research Studentship, tenable for three years and leading to the degree of PhD Candidates should hold at least an upper second class honours degree in Physics, Metallurgy or Chemistry

Applications in each case (quoting R20/72) should be addressed to Dr D J Fabian, Department of Metallurgy, University of Strathclyde, Colville Building, 48 Portland Street, Glasgow G1 1XM, stating clearly post in which interested

(52)

UNIVERSITY OF STRATHCLYDE
DEPARTMENT OF PURE AND APPLIED CHEMISTRY

Postdoctoral Research Fellowship

Applications are invited for a British Empire Cancer Campaign supported Postdoctoral Research Fellowship in Organic Chemistry The project will involve synthetic studies on hydroxybenzo cycloheptenes which show anti-leukaemic properties

The appointment, which is for one year in the first instance, will carry a salary of up to £1,923 per annum depending on experience and will commence in October, 1973

Applicants should send a full curriculum vitae as soon as possible (quoting R21/73) to Dr G R Proctor, Department of Pure and Applied Chemistry, University of Strathclyde, Thomas Graham Building, 295 Cathedral Street, Glasgow G1 1XL

(51)

HARWELL

Materials Research

A limited number of three year Research Fellowships and permanent appointments are available at Harwell for basic and applied research in materials Interesting problems being investigated in depth include fracture, radiation damage, corrosion and the development of new alloys, ceramics and composite materials The laboratory provides excellent research facilities and a stimulating working atmosphere

Candidates at first degree, doctorate or post-doctorate level will be considered for these posts Selection standards are high and candidates must have both originality and the ability to exploit sophisticated and novel techniques

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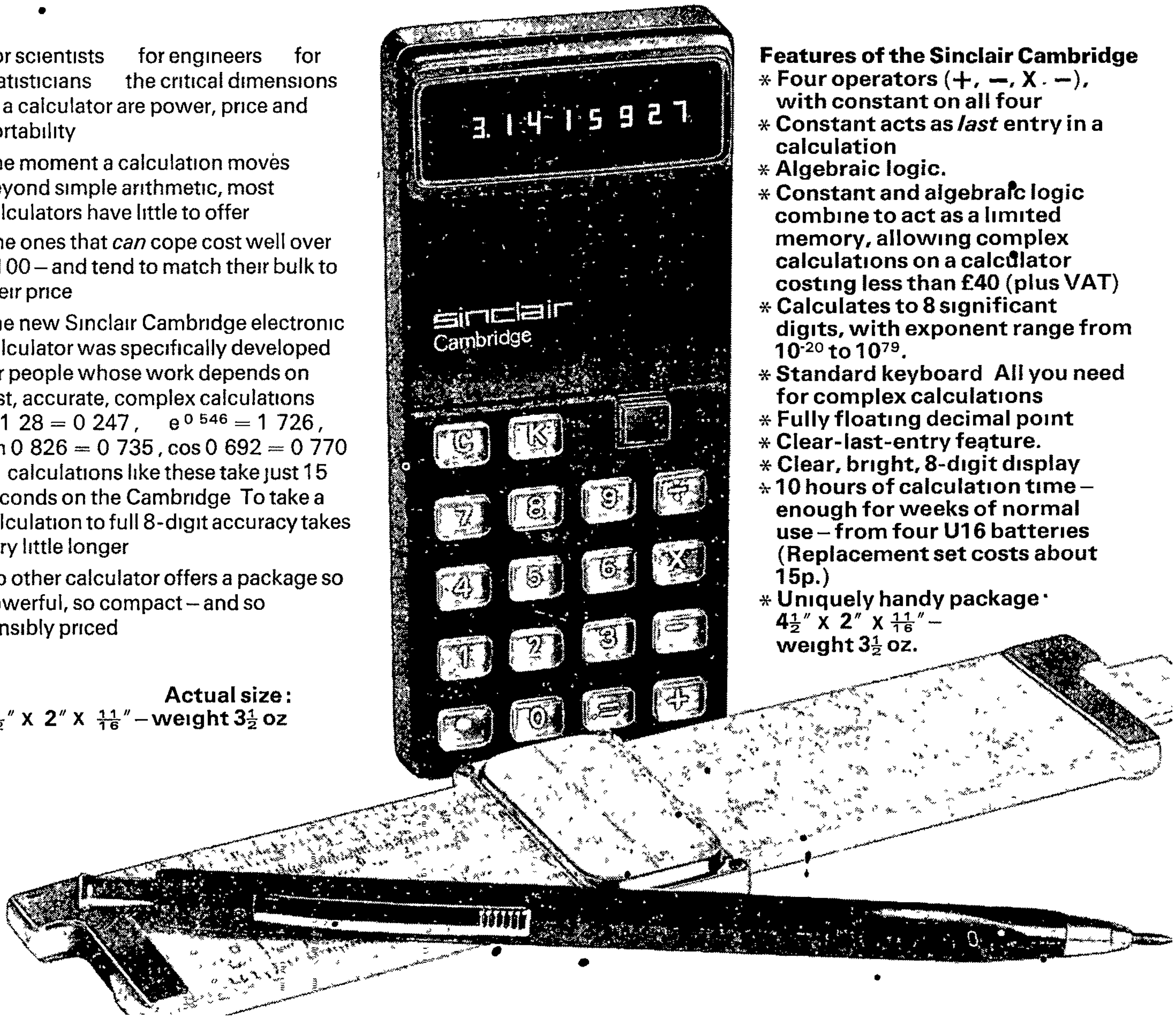

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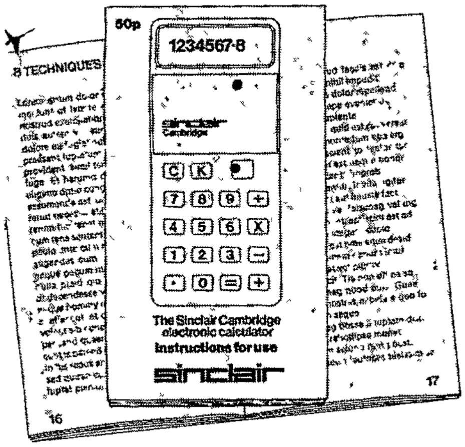
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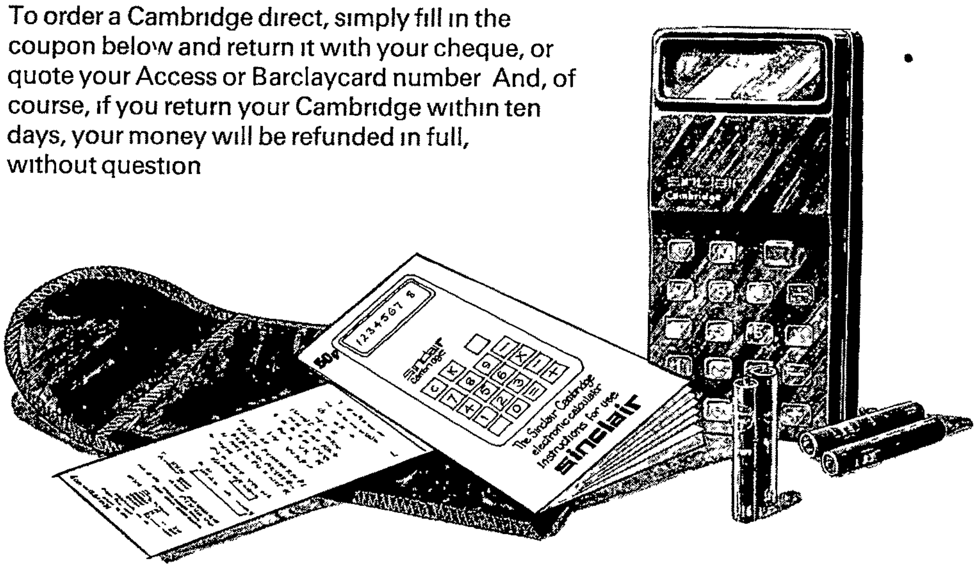
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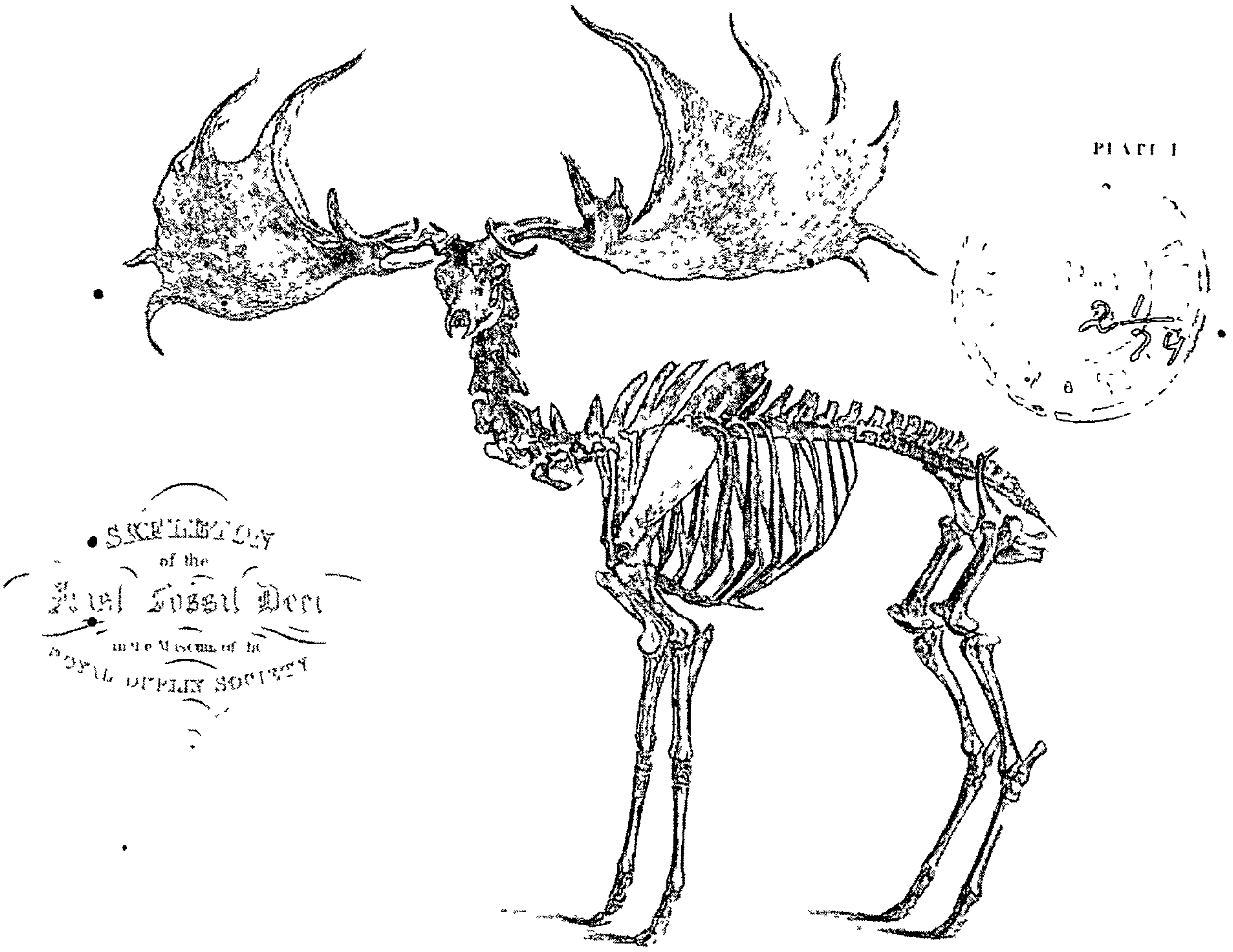

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Pipeline Blockage Cleared by House of Representatives

UNDER the pressure of intense lobbying from the oil industry and from the Administration, members of the US House of Representatives last week followed the lead of their colleagues in the Senate by passing a reckless piece of legislation. By a vote of 356 to 60, the House cleared all legal challenges to construction of the trans-Alaska oil pipeline and brushed aside the suggestion that a thorough study should be conducted of an alternative route across Canada to the US Midwest. By passing the bill the House attempted to usurp the power of the courts by deciding for them that the Department of Interior has fulfilled the mandate of the National Environmental Policy Act (NEPA) in granting a right of way for the pipeline. It is the latter provision which is not only unwise but also unnecessary, and which threatens to undermine one of the most important environmental laws in the United States.

The trans-Alaska pipeline, a proposal to transport crude oil from Alaska's North Slope to the ice-free port of Valdez, has been snarled in legal tangles for more than three years. It may thus seem contradictory to refer to Congress's actions as reckless, but members of Congress were stampeded into passing a highly questionable piece of legislation by threats of the energy crisis.

In short, both the House of Representatives and the Senate have now passed bills which clear away a particular legal technicality which was barring the way to construction of the pipeline. But, instead of stopping there and allowing the courts to decide other outstanding legal issues, supporters of the pipeline also added a provision to the bills which attempts to decide those other legal issues for the courts.

Environmentalist groups have, during the past three years, fought a long court battle against construction of the pipeline, arguing that the Secretary of the Interior has not fulfilled all the dictates of NEPA. The act requires all departments and agencies of the federal government to produce environmental impact statements giving details of the effects on the environment of proposed projects, and analysing alternatives to the proposed course of action. Opponents of the trans-Alaska pipeline have argued in the courts that the Secretary of the Interior has failed to meet the obligations of NEPA, chiefly because insufficient attention has been paid to an alternative route through Canada. They lost their case in a federal court, but appealed the ruling, and in February this year an appeals court astonished everybody by revealing that the Minerals Leasing Act of 1920 forbids the granting of a right of way wide enough for construction of the pipeline. At that time the appeals court decided not to rule on the environmental questions until the Mineral Leasing Act had been modified, and that was the chief purpose of the legislation passed last week.

The provision exempting the pipeline from further court review under NEPA was inserted into the Senate bill in the form of an amendment offered by the two Senators from Alaska, Ted Stevens and Mike Gravel. The amendment was finally agreed to by the Senate by a vote of 49 to 48, after it had been vigorously opposed by Senator Henry M. Jackson, one of the chief supporters of the trans-Alaska pipeline. Similarly, it was inserted into the House bill by a majority of one in the Interior Committee, and survived a test on the House floor by 221 votes to 198.

NEPA has been used by environmentalists to oppose a variety of government projects, and it has been responsible for a number of significant improvements in the design of projects and in the development of government policies. The act, for example, provided the level for forcing the Atomic Energy Commission to take into account environmental factors other than radiation in the licensing of power plants, and it is also likely ultimately to force cancellation of the extremely dubious attempts to free trapped natural gas with nuclear explosives. Moreover, the court suit filed under NEPA against the trans-Alaska pipeline has unquestionably forced the oil companies to adopt a much more acceptable design for the venture.

Actions which may lead to weakening NEPA are thus not to be taken lightly, but in its cavalier approach to the legal obstacles lying in the path of the pipeline, Congress has set an unfortunate precedent. Can it not be argued, for example, that because the breeder reactor will be so vital to providing energy in the 1990s, that it, too, should be exempted from NEPA review?

Equally important, in trying to deny further environmental review of the pipeline, Congress has cut off consideration of an alternative route through Canada. There are, clearly, many drawbacks to the Canadian route, including the ambivalent attitude of the Canadian government, but as it is almost certain that a gas pipeline will be built from the North Slope through Canada to the US midwest, there is a case for studying the impact of running an oil and gas line side by side. Congress, however, was persuaded by skilful lobbying from the oil industry, that the energy crisis demands not only that Alaskan oil should reach the markets without delay, but that the need is great enough to call for unwise action.

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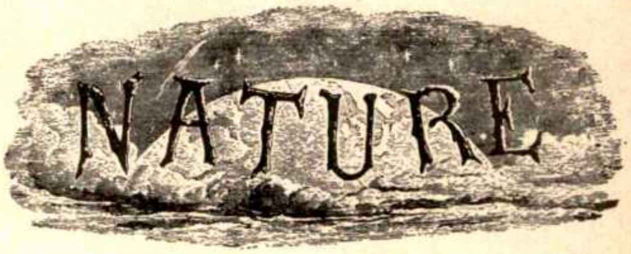
100 Years Ago



A GREAT earthquake occurred at Valparaiso early on the morning of July 8. There were six shocks in succession. Many families took refuge in the streets, the damage to private houses as well as to the public buildings being considerable; and many deaths were reported. A statue lately erected to Lord Cochrane was wheeled half round on its pedestal. The earthquake was observed to come from the east, and was felt as far south as Curico.

From *Nature* **8**, 314, August 14, 1873.

OLD WORLD

European Space Out of the Wood?

LAST week's meeting in Brussels of the European aerospace ministers, in spite of its long hours and histrionic delays, could prove a major advance in European space history. But the ministers and their civil servants are not yet out of the woods.

The agreement that finally emerged provides for Mr Michael Heseltine's European Space Agency to come into existence on April 1 next year (three months later than originally planned) and sets out—at last—which projects are going to be supported and by whom. Spacelab, L-3S (the French launcher), and MAROTS, the maritime satellite that the European Space Research Organization has been studying, are the projects that have been given the European blessing, and in the end all the nations agreed to contribute to all three projects—the only reservations being that Italy, Denmark, Sweden and Norway have still to decide on the amount of their contributions.

Feeling in the European aerospace industry is chiefly one of relief that a clear programme is finally emerging. It has been said, however, that in working to get the new agency set up, Mr Michael Heseltine, Britain's Minister for Aerospace and Shipping, has given too much away in terms of real projects. The British proposal to build a Geostationary Technology Satellite as a prototype maritime satellite was dropped in favour of MAROTS (see *Nature*, **243**, 181 ; 1973), and Britain has even agreed to contribute a largely nominal sum (2.6%) to the French launcher programme. The feeling in Whitehall, however, is that the establishment of the agency is the key point, and any contribution to the L-3S is less an important change of principle than a minor concession made to ensure that the agency gets off the ground. When the project gets under way Britain will not be a formal partner to the programme. Britain's attitude through the last few ministerial meetings has been that it is more important to plan for a rational future than to win short term victories over particular projects that may damage the long term interests of a concerted European space effort.

British expenditure in space in fact is going to be small over the next few years—a mere £30 million or so—and a large share of that—about £17 million—will be spent on MAROTS as Britain is to pick up 56% of that bill.

The problems left to be resolved are the extent of the Italian and Scandinavian contributions, the precise machinery under which the new agency will operate, and—most importantly—the way in which new projects, which in the old days would have been national projects, are to be integrated into the new organization.

The agreement for Europe to go ahead with the £130 million Spacelab project will now be signed on August 14, although there will be a reservation written in that the agreement is void if the countries that have still to decide their contributions to the overall package fail to provide the necessary funds by September 18, the deadline that was set for them at Brussels. There is, however, surprising confidence in European space circles that the money will be found. Considerable pressure will be put on the Italians in particular not to destroy an agreement that has taken months to negotiate. Even if there is a shortfall, it is felt that the countries that are already committed will increase their contributions.

The precise machinery of the new agency has still to be worked out, but it is already clearly understood that it will have a strong central management on the lines of ESRO rather than on the lines that helped lead ELDO to ruin.

Britain's chief aim in all this will be to see that all new projects dreamt up in the future will be offered to the new agency. This is one of the reasons why the national GTS programme was dropped in favour of the admittedly British dominated MAROTS programme. Another reason is that if money is to be made out of applications satellites they need to be run on a multinational basis.

SCIENCE POLICY

Dahrendorf's Solution

PROFESSOR Ralf Dahrendorf, European Commissioner for Scientific Research and Education, has produced his plans for coordinating the science and technology policies of the nine community members. Headstone of the six point plan is a new committee for Scientific and Technical Research (CREST) to add to the other acronyms that already litter the European research scene.

If approved by the council of ministers at their October meeting this committee—whose recommendations in its early years at least will not be binding—will have the task of coordinating national policies by pinpointing the areas into which each country should put more, or less, effort. The precise form the committee will take is still under discussion. If the ministers do accept the proposals—and given the fate that met Commissioner Spinelli's proposals (see *Nature*, **243**, 128 ; 1973) this can by no means be certain—it will mean that Europe finally will have a common research policy.

The other chief points in the plan allow for the commission to take a share in the proposed European Science Foundation that is currently being put together by the academies and research councils of Europe. Although no sum has been mentioned it is possible that the commission will put a small amount of money into the new body each year—perhaps 200,000 units of account (£80,000)—in order to gain the right to be involved. Professor Dahrendorf has also highlighted a series of projects that he is asking the council of ministers to approve. These include studies on medical and social research, energy policy—including direct conversion, the transport of energy and environmental and regional energy policies—as well as an industrial policy that includes work on materials and computers.

Where this work is to be done has not yet been decided, but possibly contracts would be placed in industry, national research institutes and the community's Joint Research Centre.

The programme includes some old favourites of proposed European cooperation such as a community-wide scientific information network and the setting up of a European bureau of standards based around the existing Bureau of Nuclear Standards at Geel in Belgium. The new bureau, however, would have far wider interests, covering for example standards in pharmaceuticals and medicine, in food conservation, pesticides and telephone and telecommunications links.

The final point in the proposal is that the commission should join the futures business by setting up a group to examine likely developments in the next thirty years along the lines of the MIT and Club of Rome studies. The group has been dubbed "Europe+30".

If the council of ministers accepts the proposals it is likely that the PREST group that advises the council of ministers will be dissolved, but the recently set up CERD group, whose purpose is to advise the commission on the policies it should adopt, will continue in existence.

BUSINESS

Nuclear Trading

A PLEASANT past and a promising future characterizes the annual reports of British Nuclear Fuels and The Radiochemical Centre, published last week.

These two off-shoots of the United Kingdom Atomic Energy Authority have just celebrated their second year as independent entities, and both are now operating at a healthy profit. But British Nuclear Fuels report is noteworthy chiefly for the news that the government is to advance the greater part of the capital required to build the gas centrifuge uranium enrichment plant that is currently planned for completion in 1976. Under a tripartite agreement between Britain, West Germany and the Netherlands two demonstration plants designed to produce 200 tonnes a year are being built at Capenhurst and Almelo to be run by Urenco and Centec, the two companies set up under the agreement to construct the plants. If all goes well enrichment capacity will be increased to 2,000 tonnes a year by 1980.

As Sir John Hill, BNFL's chairman, points out in the report, the capital sum—which is undisclosed but is thought to total between £50 and £60 million—is substantial in relation of BNFL's earnings, which last year rose £1 million to £65 million. In spite of the three way sharing of construction costs the sum is still large, under the terms of the guarantee the government will be repaid out of the profits from the undertaking.

The report also states that BNFL will not be taking part in the second stage of the French Eurodif studies of diffusion plant. France is eager to build a large diffusion plant, but the economics of the operation are such that only one large plant that is run at almost full load can be built. BNFL took part in the first stage of the international studies of such a plant but declare that "the first year's work ... confirmed the company in its view that the centrifuge process was likely to offer better prospects of producing enrichment for the European and world market at competitive prices in the medium and long term. The company is not taking part in the second year of the study".

The report also shows that BNFL's profits remained static at £10 million although the percentage profit rose by 1.7% to 15.8%. Sales only increased £1.6 million, chiefly due to the lack of new orders for nuclear power stations and the fact that the Advanced Gas Cooled Reactors are not yet on load. BNFL managed to sell some reload fuel for light water reactors to the Netherlands, "but a major expansion in this field is unlikely unless water reactors are introduced into the UK power programme", according to Sir John Hill.

The Radiochemical Centre for its part increased its sales by over 25% to £7.6 million. The profit before tax rose 61% to £1.3 million, representing a return on capital after loan interest charges of 28%. Seventy per cent of the centre's business is overseas, the largest growth area being radiopharmaceuticals.

Considerable investment in new facilities is planned over the next few years, and the centre's chairman, Sir Charles Cunningham, states that the company's staff structure—essentially that inherited from the United Kingdom Atomic Energy Authority—is to be revamped "to meet the needs of a commercial company operating in world markets".

ECOLOGY

Detecting the Changes

from a Correspondent

How is environmental change (brought about by man's activities or by natural causes) to be assessed? This broad question received a detailed examination in London recently when the Natural Environment Research Council held a one day seminar under the title the detection and assessment of significant biological change.

The meeting's conclusion seemed chiefly to be that there is a great need for more background data, more scientific effort and, of course, more resources. But on the way to that conclusion some interesting points were raised.

Mr R. J. H. Beverton, secretary of NERC, highlighted the problem by pointing out that one of the chief difficulties lies in the diversity of the living world and in its, mostly unrecorded, variability. As many man-made influences are enhancements of natural ones it follows that their effects are difficult to detect and quantify. It is often difficult, Mr Beverton said, to distinguish between the signal and the background noise.

Many monitoring programmes are already under way whose objective is to detect adverse trends. The methods employed are almost always physical or chemical—for instance measuring temperature, salinity, dissolved oxygen or suspended solids. The question is how important are the changes to biological communities, and how can these fluctuations be detected before damage occurs?

Dr J. W. G. Lund of the Freshwater Biological Association declared that while it is often possible, with hindsight, to explain changes that have already taken place in the freshwater environment, it is quite a different matter to predict them. Often, he said, we do not even know what should be observed. This view was supported by Dr J. M. Hellawell who, as a NERC research fellow, has examined several schemes for biological monitoring of rivers. He concluded that the schemes he studied were often inaccurate and sometimes misleading when taken on their own.

Predicting changes on land seems little easier. Schemes for aphid and moth monitoring that have been run on a national scale for a number of years were described by Dr L. R. Taylor of the Rothamsted research station. Again, changes are easily detected in the populations, but it is so far impossible to distinguish between short and long term climatic changes, alterations in land use or other man-made influences.

In the marine environment changes cannot yet be predicted accurately, while on the shoreline too little is known about the biological interactions in shore communities to allow monitoring to take place.

Other monitoring programmes run into further difficulties over the subjective element introduced by the observers who provide the data—for example the monitoring of bird populations by the British Trust for Ornithology and the mapping of plant species from Monks Wood research station.

For monitoring to be effective it may, in the end, have to concentrate on a limited closely defined objective. Nonetheless it is still hoped that some schemes can be conceived to provide an overall index of environmental quality. In response to this possibility NERC has just appointed two working groups to examine biological surveillance in the marine and terrestrial environments.

SPACE

Mars 6 Stirs Speculation

from our Cosmology Correspondent

THE launch of Mars 6 on August 6, just one day before the recent "window" for Mars launches closed, makes the present series of probes the first Soviet triple venture to the red planet. Together with the wording of official communiqués about the launch, this has encouraged renewed speculation that Mars 6 might be the awaited soft lander, possibly carrying a "Marsokhod".

While Mars 4 and Mars 5 are described as being "analogous in structure and purpose" (see *Nature*, **244**, 249, 1973), Mars 6 is different in design from the two probes now three weeks ahead of it on the way to Mars, according to TASS. The official releases say that Mars 6 will use Mars 4 in carrying out its exploration, a choice of phrase which has been taken as hinting strongly that Mars 6 will carry out a landing on the planet and use Mars 4 to relay messages back to Earth. In that case, Mars 5 might well incorporate a backup facility for Mars 4.

NEW WORLD

Advice of NIH Officials Ignored

by our Washington Correspondent

A SERIES of memoranda which surfaced last week on Capitol Hill provide a fascinating glimpse of executive infighting which preceded the recent cutbacks in funding for biomedical research Written late last year by Dr Robert Q Marston, then Director of the National Institutes of Health, and Dr Frank J. Rauscher, Jun , Director of the National Cancer Institute, the memoranda show that the advice of top NIH officials was completely ignored by the Office of Management and Budget, and they also bear witness to the strong, independent stand taken by Dr Marston before he was fired as NIH director in January

The memoranda were made public by Senator Mike Mansfield, the Senate Majority Leader, and Senator Warren G Magnuson, chairman of the appropriations subcommittee which deals with the NIH budget In releasing them, the two senators are clearly marking out the battle lines for yet another struggle between Congress and the Administration over the size of the budget for the Department of Health, Education and Welfare—four times in the past four years Congress has passed HEW appropriations bills which President Nixon has vetoed because he considered them to be inflationary, and it is likely that the same thing will happen again this year

Late last year, when it became clear that federal expenditure was greatly outstripping revenues, President Nixon instructed the OMB to cut back on expenditures in order to head off a tax increase The National Institutes of Health were particularly hard hit by the squeeze, for the OMB proposed to apply the knife not only to planned expenditures in the 1974 budget, which was then in the final stages of preparation, but also to 1973 expenditures The proposal was to reduce the budgets of all the institutes except for the National Cancer Institute (NCI) and the National Heart and Lung Institute (NHLI), both of which were too politically sensitive to cut, and to eliminate entirely the NIH training and fellowship programmes.

When that proposal was put to Dr Marston, he fired off a memorandum to the Secretary of Health, Education and Welfare deploring the cuts and suggesting that "the President should be made aware of the long-range impact that this will have to the health of the Nation" The memorandum, dated December 19, pointed out that Marston had previously expressed concern that increases in the budgets of NCI and NHLI were being made at the expense of other institutes, and added that the final OMB proposals "would mean a program over a two-year period from fiscal year 1972 to fiscal year 1974 where cancer increases by $127 million, heart increases by $23 million and the rest of biomedical research *decreases* by $111 million — this, in spite of assurances that the highly political and visible programs would not grow at the expense of basic programs" As for training programmes, Marston acknowledged in the memorandum that they had been axed by OMB in spite of opposition from NIH officials and from the Secretary of HEW

In spite of the fact that the National Cancer Institute escaped from the budgetary squeeze with an increase of funds, however, it is clear from two memoranda written by Dr Rauscher that the institute suffered badly from OMB's knife NCI officials originally put in a budget request for the 1974 fiscal year of $640 million, with the objective of increasing the cancer research budget to $1,000 million over the next few years. Clearly, the $640 million was an opening bid in the negotiations between NCI and OMB, and NCI officials knew that they would not get everything they wanted. But they were not expecting the request to be trimmed to $500 million, which eventually happened

Asked in November to highlight the consequences if NCI's budget request were cut from $640 million to $456 or $550 million, Rauscher said in a memorandum to OMB that "a significant decrease from the $640 million, which we have requested for 1974, will seriously limit NCI's ability to carry out the objectives the Executive and members of Congress have so often enunciated" Among the consequences of a budget of $550 million that Rauscher lists in the memorandum are restriction of the "expansion of immunologic treatment of cancer into clinical trials", at least a year's delay in letting industrial contracts to produce automated screening of Pap tests, "instead of introducing 8 to 10 new antitumour agents into general medical practice, at best we could introduce only 5 or 6", efforts to develop less hazardous cigarettes would have to be cut back or terminated, plans to expand cancer research at Fort Detrick "cannot be implemented", and "a deep cut would be necessary in the construction program in order to preclude major reductions in the ongoing program of competing renewal and new grants" In the event, however, OMB ignored Rauscher's plea and cut the NCI budget request to $500 million.

Congress has not yet completed action on the 1974 budget for the Department of Health, Education and Welfare, but it is already clear that it will greatly increase the Administration's request The House of Representatives, for example, has passed an appropriations bill that is some $1,800 million greater than President Nixon requested, and to judge by the comments made by Magnuson last week, the Senate is likely to follow suite Clearly, the HEW budget is again destined to become a political football

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FUNDING

No Money Yet

by our Washington Correspondent

CONGRESS adjourned last week without completing action on any major appropriations bills affecting science and technology But at least NASA and the National Science Foundation can be reasonably certain of how much money Congress is willing to give them, for the Appropriations Bill, alotting funds to those two agencies, has now been pased by the House of Representatives and will probably be taken up by the Senate early in September There are still some minor disagreements to be sorted out on the Senate floor, but NASA is likely to end up with some $3,002 million—$13 9 million less than the Administration requested—and the National Science Foundation is likely to get $569 6 million—$13 million less than the administration requested

Those figures were contained in a conference report which settled differences in the Appropriations Bills passed earlier this year by the House of Representatives and the Senate The House passed the conference report shortly before the adjournment, but the Senate did not act on it because it contains two controversial provisions, unrelated to the two science agencies, which require some debate At least astronomers can be thankful for one thing—the conference report includes $5 million for the Very Large Array Telescope System Although that figure is only half of the original budget request, the House of Representatives had originally cut out all the money for the VLA and restoration of half the request will at least allow construction to start this year

AIR POLLUTION

Detroit Blues

by our Washington Correspondent

AUTOMOBILE manufacturers last week wrung another concession out of the Environmental Protection Agency. But, to judge by the volume of complaints from Detroit, the EPA's concession fell well short of capitulation. Mr Robert Fri, acting EPA Administrator, announced that he has granted the manufacturers their request for an extra year to meet stringent limits on the amount of oxides of nitrogen in car exhausts, but he also set interim limits which the manufacturers insist are still too tough.

The decision parallels an earlier, controversial decision taken by Mr Ruckelshaus when he was administrator of EPA, to allow the manufacturers an extra year to meet emissions standards for hydrocarbons and carbon monoxide (see *Nature*, **242**, 491, 1973). The Clean Air Act specifies that all 1976 model cars sold in the US must emit no more than 0.4 g of oxides of nitrogen per mile—about 90 per cent less than 1971 models—but it also allows the EPA Administrator to delay imposing the standards by a year if he finds that it cannot be met on time. That, essentially, is what Mr Fri decided last week, but he also imposed a limit of 2 g per mile, a limit which the agency maintains can be achieved by recirculating some of the exhaust gases through the combustion chamber.

Last week's action was widely expected, and it did not stir up the controversy that Mr Ruckelshaus's earlier decision created, chiefly because few people expect the 0.4 g limit will ever be imposed. The EPA recently released a set of figures to show that the monitoring data which led to the limit being set are incorrect—in 1970, when the Clean Air Act was passed, some 47 urban areas were reckoned to have potentially hazardous levels of nitrogen oxides in their air, but only two cities are now accorded that dubious distinction. Accordingly, the EPA will soon recommend that Congress should amend the act to relax the standard.

One incentive for relaxing the standard is that the motor manufacturers are intending to meet it by installing a second catalyst to car exhausts. The dual catalyst system would carry a large fuel penalty, which is not a good asset with talk of the energy crisis rampant.

It is not yet clear what action Congress will take, but it is likely that a final limit close to the 2 g interim standard set by Mr Fri will emerge. Why is Detroit not happy with it? According to industry spokesmen, one problem they have is that engine conditions desirable for reducing hydrocarbon and carbon monoxide emissions tend to maximize production of oxides of nitrogen, and so they are not certain that they can meet all the standards at the same time. But it should be remembered that when Mr Ruckelshaus set tough interim standards of hydrocarbons and carbon monoxide, the motor industry chorused that they were impossibly tough, but later decided that they would probably be attainable after all.

ENERGY

Canada's Policy

from a Correspondent

DURING June, the Hon Donald S. Macdonald, Minister of Energy, Mines and Resources, tabled in the Canadian House of Commons a document entitled *An Energy Policy for Canada*. The government now hopes that the stage is set for a debate on an overall energy policy rather than a consideration of a number of fuel policies as was the case in the past.

Canada is in a unique position among the industrialized nations because its own resources are sufficient to meet current and projected needs. It is thus quite feasible to defer some of the resource development to serve the needs of future generations. There are, however, at least three pressures against this alternative. The first is the desire to increase the cash flow and thus to derive greater economic benefits for the present generation of Canadians. The second is geopolitical. Canada, if it chose this alternative, would be the first non-OPEC country to propose to leave its wealth in the ground. Although Canada now supplies about 22% of USA imports of energy, the rising demands of USA economy would have to be met by oil imports from North Africa and the Middle East, and Canada's relative importance would decrease. Third, there is a real fear that if Canada's oil is not sold now, future energy shortages will force development of alternate supplies (nuclear, solar, geothermal, for example) of energy, and the markets for northern oil will vanish. Irrational as this fear must be, it is based on a still fresh memory of the 1950s when Alberta oil could not be given away which led to the 1961 Energy Policy which prohibited cheap foreign crude oil being imported through eastern ports thus forcing industrialized Ontario to use Alberta oil and gas.

Recognizing the complexity of interlocking constraints, the energy studies document puts a strong emphasis on the requirement for a solid science base. "Priority considerations refer to what is generally defined as research and development. A major priority outside the limits of this specific activity is the improvement of our basic knowledge of the extent, accessibility and quality of the resource base. If this basic information is inaccurate or incomplete, all of our planning and policy development is of dubious value."

The document even goes as far as to give a list of priorities for different scientific activities—which is more than a majority of recent science policy studies were prepared to do. The present research effort appears to be lopsided. A preliminary review of federal research and development expenditure on energy in 1971 showed that 71% went into nuclear energy research, while only 11% was spent on oil and gas. As there is no national (state) petroleum company little petroleum research is done in Canada. The report argues at some length that the establishment of a fully integrated National Petroleum Company would automatically improve matters.

In view of the large predicted reserves of oil in Athabasca tar sands (almost twice as much as the total of all other predicted ultimate recoverable reserves of oil and gas in Canada) research on exploitation of this resource is highlighted as the top priority. The extraction at present is only slightly larger than a pilot plant operation and only 0.1% of Federal research and development funds were spent on this in 1971.

The second research priority is to do with techniques and equipment for exploration, production and transportation of hydrocarbons in the Arctic and offshore regions of the continental shelves.

The third priority is the energy resource inventory appraisal. The results of these investigations, however, are critically dependent both on methodology and initial assumptions. Appraisal is further complicated by the fact that inputs from geology, production engineering and market economics must be blended before meaningful estimates can be made.

In the long run the report recognizes the importance of nuclear energy and is reasonably satisfied with the successful design of the CANDU reactor which does not require enriched uranium, but needs heavy water.

The report, however, is conventional and old fashioned in outlook. With its emphasis on growth and continuing expansion of demand, it conveys an impression that the majority of studies were undertaken in the early 1960s, before all the debates generated by Limits to Growth.

At the same time, enough alternative options are raised to give all interested groups an opportunity to voice their opinions and objections. It is to be hoped that it is not just a naive wish that the due regard for the democratic process will give Canadians an energy policy of their choice.

NEWS AND VIEWS

Value of a Hypothesis

PROFESSOR P A STURROCK of Stanford University has published a paper on scientific inference in the *Astrophysical Journal* (**182**, 569, 1973) His object is to evaluate various hypotheses concerning a class of object in the light of several sets of observations upon members of the class, with special reference to applications of astrophysical interest

Suppose we have a mixed bag of equal large numbers of black and white balls, and suppose two balls are abstracted at random Consider the hypothesis, H, that these are two black balls On the background knowledge supplied, the (prior) probability that H is valid is one-quarter Suppose then that one ball of this pair is looked at and seen to be black, with this additional observational information, the (post) probability that H is valid (the "value" of the hypothesis) is one-half, if one of the pair is looked at and seen to be white, the post probability of H is zero The theorem giving the general relation between post- and prior-probabilities is Bayes's rule

In a broad sense, Sturrock produces a generalization of this rule He illustrates his ideas using the case of pulsars, taking as hypotheses that a pulsar is (H_1) a rotating neutron star, (H_2) a pulsating white dwarf, (H_0) an object of some other sort What he calls "items" in this example concern pulsed radio emission, range of periods, change of period, association with supernovae, photospheric radiation, power in the case of the Crab pulsar

The novel feature of Sturrock's treatment is his concept of the "interface" between observation and theory In any application, the interface consists of several "items" Each item consists of a set of statements about some feature, one and only one of which must be true in the example the item about change of periods consists of the three statements all pulsars slow down, all pulsars speed up, neither of these is true Using the available particular observations, and whatever background information is relevant, the "observer" estimates a probability that each statement is true

The hypotheses to be evaluated have to form a complete and mutually exclusive set To them the "theorist" assigns prior probabilities, then he estimates the probability on each hypothesis that each statement in an item is true The same background information is available to him, but he is supposed to know nothing about the observations special to the problem Assuming the truth of any statement, and using Bayes's rule, the theorist can then evaluate the (post) probability for each hypothesis Combining this with the observer's estimate of the probability of each statement, the theorist then obtains the post probability of the hypothesis so far as one entire item is concerned Sturrock finally gives the (non-trivial) combination of such results for any number of items.

Contact between observation and theory occurs only at the interface of statements The observer estimates the probabilities that certain fairly general statements are valid in the light of the observational material, as Sturrock says, these estimates must be without theoretical bias. The theorist estimates the probabilities that his hypotheses are valid if one or another of the statements is valid, these estimates must be without observational bias Then the two sets of probabilities meet at the interface and produce the evaluations This formalizes the procedure presumably followed, implicitly and unsystematically, in observational science in general

In order to follow Sturrock's procedure, the reader needs to study his example on pulsars He gives it for illustration only, but it is remarkable that some four years ago he got for the post probabilities based on all items for neutron star 0 995, white dwarf 10^{-8}, some other object 0 005

Sturrock is disarmingly candid about the several basic difficulties of such work which he explicitly refrains from examining in his paper In particular, there are two inter-related weaknesses, the need for the "null" or "ignorance" hypothesis (H_0 in the example) and the subjective character of the assigned probabilities

Significance may be placed upon the probabilities of the other hypotheses relative to the null hypothesis only on the subjective impression that one has been generous to the null hypothesis As regards the probabilities of the other hypotheses relative to each other, however, under certain circumstances it may be possible to demonstrate that these are insensitive assumptions about the null hypothesis

In its present formulation, Sturrock's work would apply only to the standard detective-story type of problem where the observer (policeman) and the theorist ("Poirot") have to choose one of several given suspects or the possibility of an "outside job" The detective story-teller's aim is to keep all subjective probabilities about equal until some crucial item comes along One thing to be learned from Sturrock, however, is that, even if each available item is inconclusive in itself, the resultant effect of several items may give almost completely convincing support for one solution This would be expected, but it is highly interesting to see Sturrock's quantitative illustration But again there is still the subjective element, well recognized in detective fiction at the stage when "Poirot" knows the culprit but still has no case for a court of law

Most astrophysical problems for most of the time are not detective problems of this sort, and the scope for the full application of such work is obviously restricted Nevertheless it may have value in several ways first, it may help to classify the activities of various investigators, each of whom may be said to be trying to evaluate any one of Sturrock's probabilities in regard to some current problem, and so to clarify the purposes of the investigations, second, it should show which items of observation might be expected to have most significance for the solution of the problem, third, in a large class of problems, it seems to be the aim ultimately to reach a stage when Sturrock's type of evaluation is needed—implicitly or explicitly—and it may expedite a decision to make it explicit On the other hand, there are large parts of astrophysics where it would probably be an arid proceeding to try and impose such an analysis In any event, Sturrock has made a valiant effort to bring order into the haphazard procedures of most astrophysicists

W H McC

An Alternative to Mantle Plumes

THE bulk of the world's seismic, volcanic, orogenic and large-scale tectonic activity takes place along relatively narrow bands which form a linked pattern around the Earth's surface. The discovery of this pattern played its own important part in the formulation of the new global tectonics, and conversely, it is within the framework of global tectonic theory that the active bands are seen to have physical, rather than simply observational, significance. For the bands define lithospheric plate margins—zones where lithosphere is created, where it finally descends into the mantle, where it collides with other lithosphere, or where lateral motion takes place between plates in what are known as transform faults. In short, whatever else it may do, plate boundary tectonics combines into a single conceptual scheme most of the internal processes changing the face and body of the Earth's lithosphere.

But not all of them. On the ocean floor, volcanism occurs well away from plate margins, very often forming series of mountains and islands, such as the Hawaiian–Emperor chain, which are geographically and temporally linked. Within continental plates are to be found graben, rift valleys and seismic zones. In the United States, for example, a notable series of earthquakes in 1811 and 1812 drew attention to an active seismic zone near New Madrid, Missouri; indeed, the largest known American earthquake outside Alaska took place not in California, Washington or Nevada but as part of the New Madrid series. These and other phenomena may account for a relatively small proportion of the Earth's activity, but they are by no means insignificant and can hardly be dismissed as local.

In view of the influential position now occupied by plate tectonics, it would seem logical to ask how global tectonic concepts may acommodate, or be made to accommodate, important processes taking place away from plate margins. In other words, given the overall framework involving the most significant tectonic phenomena, the obvious next step would be to determine how the less significant (or apparently less significant) processes fit in. Curiously, however, this is not what seems to have happened. For reasons which historians will be left to discover, many geophysicists have chosen instead to take an inspired, intellectual and, on the face of it, illogical leap to a basically *ad hoc* explanation bearing little obvious relationship to "classical" plate tectonics. And what makes the situation even stranger, in retrospect, is that this new explanation for within-plate processes is now being heralded, in some quarters at least, as the underlying explanation for plate boundary tectonics as well. The child thus becomes father of the man.

The explanation concerned here is, of course, that involving hot spots and mantle plumes. As the debate over the existence of these phenomena is still raging, it is not yet possible to say whether the inspired leap will turn out to have led to a fundamental truth or into a scientific blind alley. In the meantime, however, few would deny that it is highly desirable that alternative mid-plate tectonic theories be put forward for consideration by Earth scientists of all persuasions. Thus whatever one's views on the validity, or otherwise, of mantle plumes, the article by Turcotte and Oxburgh on page 337 of this issue of *Nature* should be welcome.

Specifically, Turcotte and Oxburgh make out a case for explaining mid-plate tectonic phenomena in terms of crustal extension induced by tensional stresses of two types. The important point, however, is that the stresses can be seen as the logical outcome of well-known plate tectonic processes without recourse to any completely new phenomena. If science is to be regarded as a system involving the minimum of unproven assumptions, the new hypothesis put forward by Turcotte and Oxburgh will be regarded as being intrinsically more likely than mantle plumes. Unfortunately, life is not always that simple.

P. J. S.

ORIGIN OF LIFE

Could Life Start Again?

from a Correspondent

THE fascination which the question of the origin of life exerts on scientists as diverse as theoretical physicists, geologists, chemists and biologists of all descriptions, from molecular to ecological, was reflected in the contributions to the Fourth International Conference on the subject held in Barcelona from June 25–28 under the auspices of the new Autonomous University of Barcelona and the International Society for the Study of the Origin of Life (ISSOL), in order to honour the contributions made to the field by Drs A. I. Oparin (Bach Institute of Biochemistry, Moscow), H. C. Urey and M. Calvin (both of University of California). In the space of 5 days the participants tried to understand what went on from the origin of the Earth (4.6×10^9 years ago) to the end of the Precambrian era (0.7×10^9 years ago) as well as discussing recent and projected interplanetary exploration—a sterile but stimulating exercise.

To set the scene Dr D. Buhl (Radio Astronomy Observatory, W. Virginia) described the recent recognition by radio astronomers of the large clouds of organic molecules in our Galaxy. Many different compounds containing C, H, O and S have been detected but the presence of P is still in doubt. Because of the characteristics of the radio spectrum a particular molecule can be identified with 99% certainty on the basis of a single line. Clouds of organic molecules appear when a star is born, suggesting that the evolution of a molecular cloud is a significant prelude to the origin of life. There seems to be directed chemistry and not chaos in these interstellar clouds. Dr T. Owen (State University of New York) suggested that Titan, the large satellite of Saturn, may provide a model for early organic synthesis and that comets of the outer Solar System with their particular chemical composition may be the link between interstellar space and the formation of the Solar System. The possible formation of organic compounds in interstellar clouds and in meteorites by the Fischer–Tropsch type of synthesis was described by Dr E. Anders (University of Chicago). This type of synthesis can produce most of the simpler and more complex organic carbon compounds from CO, H_2, and NH_3.

The production of diverse organic compounds in abiotic conditions with different types of energy sources, for example electrical discharges, ultraviolet, heat and so on, has been known since the early 1950s and it was their discoverer (Dr S. Miller (University of San Diego, California) who presented a review on the synthesis of amino acids in simulated primitive Earth conditions. Dr J. Oró (Universities of Houston and Barcelona) described prebiotic syntheses of nucleic acid components and oligonucleotides and Dr C. Ponnamperuma (University of Maryland) suggested how small peptides and oligonucleotides may have interacted in the "primordial soup". It was suggested by Dr L. Orgel (Salk Institute, California) that longer oligomers may have been coded for so as to produce alternating hydrophobic and hydrophilic amino acids in a primitive peptide, a process for which Dr M Paecht-Horowitz (Weizmann Institute, Rehovoth) proposed a catalytic role for specific clay particles

A highlight of the meeting was the talk by Dr Oparin, who first published his ideas on the origin of life in 1924 and who was undoubtedly a progenitor (along with J B S Haldane, who published later in 1929) of most of the modern ideas in the field He stressed the multiple character of the origin of life, as opposed to the notion that it was an isolated accident So called "probionts" would be formed which undergo a natural selection allowing the survival and development of forms better adapted to the exterior environment Dr S Fox (University of Miami) then reviewed the plethora of artificially made proteinoid microspheres which have been considered as models for probionts Many simple enzymatic properties have been shown to be inherent in microspheres but now it has been found that proteinoids plus incorporated polynucleotides (protosomes) can condense individual amino acids into peptides It is proposed that the evolution of information through amino acids and protoprotein to contemporary ribosomal synthesis was continuous Heterotrophic proteinoid microspheres could have become similar to contemporary types of cells and thus form the link between abiotic organic synthesis and the first type of multifunctional cell The formation of lipoprotein membranes in the primaeval environment was described by Dr J F Danielli (Centre for Theoretical Biology, State University of New York) The primitive membrane could have evolved slowly, utilizing the basic, easily formed lipid bilayer as a model It is possible that a membrane-associated DNA could have been a primitive genetic system

Early biochemical evolution was the topic of two colloquia and symposia, which included contributions by Dr M O Dayhoff (National Biomedical Research Foundation, Georgetown University, Washington), Dr T H Jukes (University of Berkeley, California), Dr D O Hall (King's College, London), and Dr H Baltscheffsky (University of Stockholm) on the evolution of tRNA, 5S ribosomal RNA, cytochrome *c* and ferredoxin based on their known amino acid sequences So far ferredoxins are the only proteins which have been sequenced and are known to occur in all living organisms investigated The use of powerful computer techniques is helping the analysis of the sequence data which are now being correlated with biological and physico-chemical information Dr R Buvet (University of Paris) showed how compounds which undergo oxidation-reduction reactions, and possibly resembling protein active centres, can be synthesized in conditions simulating the primitive environment The role of porphyrins, especially chlorophylls, in evolution was stressed by Dr A A Krasnovsky (Bach Institute of Biochemistry, Moscow) who has shown the diversity of model and biological electron transfer reactions which can be catalysed by porphyrin-type compounds

The Precambrian fossil record was well reviewed by Drs J W Schopf (University of Los Angeles, California) and M Muir (Imperial College, London) Discoveries in this field during the past 6–7 years seem to establish that life (bacterial?) probably existed as early as 3 3$\times 10^9$ years ago and that by 2 2$\times 10^9$ years ago there was oxygen present in the Earth's atmosphere Some time in this period blue–green algae (prokaryotes) which could evolve oxygen developed, and there are now intimations that multicellular and colonial forms of organisms (possibly algal eukaryotes) may have existed as early as 1 9 to 1 6$\times 10^9$ years ago

Finally, there was a session on planetary exploration and exobiology wherein the 1975 NASA Viking mission to Mars was explained Biological experiments, calculated to allow for possible misconceptions of the nature of life on Mars, will be conducted to assay *in situ* the possibility of its existence Dr G Eglinton (University of Bristol) expressed some optimism for an automatically-returned 1 kg sample from Mars by 1985 In view of all the concern about life in the extreme conditions of space systems and on the primitive Earth, it was salutary to hear Dr W V Vishniac (University of Rochester) speak on life in an extreme environment on Earth—to be precise, in a desert called Wright Valley in Antarctica where the average humidity is only 10% and the summer air temperatures are −5 to −15° C In these severe conditions of lack of water (a few monolayers of water adsorbed on soil particles) some growth and metabolic activity of bacteria and actinomycete-like organisms does occur. Live bacteria were even detected at a depth of 40 cm in the frozen ice Why go to Mars?

CONTRACTILE SYSTEMS

Primaeval Twitch

from our Molecular Biology Correspondent

APART from relatively minor modifications every few millenia, nature's original model for an engine to turn chemical energy into motion can be adjudged to have survived the caprices of evolutionary fashion In the most advanced form, the contractile components, actin and myosin, are organized within separate filaments, and are associated also with a system of proteins responsible for modulating activation by calcium ions injected from the surrounding membrane In more primitive models there is a less obviously purposeful interaction in an essentially amorphous sludge The evolutionary pressures have acted almost entirely on the more complex and specialized component of the contractile mechanism, myosin, which differs appreciably from organism to organism, and even from muscle to muscle, whereas the actin is always much the same As Szent-Gyorgyi and his colleagues have shown, for example, the myosin in the muscles of the most primitive animals itself embodies the calcium-sensitive control system The myosin from unicellular creatures, such as the slime mould, is nevertheless remarkably similar in most essential respects to that of mammalian muscles That of the soil amoeba has now been isolated and characterized, and shows some curious, and so far unparalleled, structural features

Pollard and Korn (*J biol Chem*, **248**, 4682, 1973) used the potassium-EDTA ATPase, which is unique to myosin, to track down the myosin of *Acanthamoeba* This activity remained in the supernatant from the homogenates, whereas mitochondrial and membrane magnesium-ATPases were carried down in the pellet Successive purification steps, involving precipitation and chromatography, led to a substantially pure product, which unlike muscle myosin was soluble at low ionic strength The ATPase activity was of a similar order to that of muscle myosin, and was inhibited by magnesium but unaffected by calcium Like muscle myosin the *Acanthamoeba* protein contains heavy chains, and also light chains, two in number and judged by gel electrophoresis in SDS to have molecular weights of 14,000 and 16,000 The evidence concerning the molecular weight of the whole molecule is circumstantial In SDS electrophoresis the heavy chains come out at 140,000 Pollard and Korn then argue that since the elution volume in a gel filtration experiment on the native protein is no higher than would correspond to a globular protein of about 150,000, rather than to a highly disymmetric species like muscle myosin, such a value must represent an upper limit for the molecular weight They infer therefore that their protein consists of a single heavy chain of 140,000, with two light chains It forms no filamentous aggregates, and its amino acid composition has little in common with that of other myosins The lugubrious response of a protein chemist, confronted with these data, will undoubtedly be to question whether the preparations might represent nothing more than proteolytic fragments of some more respectable myosin-like myosin, he will be bound to concede, however, that Pollard and Korn have made every effort to eliminate this possibility They have shown that the properties and the yield of their protein are unaffected by increasing time intervals between homogenization and fractionation, that no ninhydrin-responsive material is generated during the preparation, so that no significant proteolytic activity is in evidence in the homogenate, and that muscle myosin is not broken down on incubation with the same homogenates

In a companion paper (*ibid*, 4691) Pollard and Korn go on to characterize the interaction of *Acanthamoeba* myosin with actin F actin activates the ATPase of the myosin, and in the absence of ATP carries it down when in the ultracentrifuge In the electron microscope there is little evidence of the formation of the characteristic arrowheads on the actin filaments, perhaps in consequence of the apparently symmetrical shape of the myosin, but the helical repeat of the actin filaments is reinforced and there is increased clustering of the filaments A unique feature of the interaction is its apparent requirement for a cofactor This was discovered because at the final stage of purification the actin-dependence of the ATPase activity vanished The cofactor has been isolated, and is evidently a protein with a molecular weight of some 100,000 Its efficacy is not sensitive to calcium, and there are some unexplained features in the manner in which it operates

The extensive similarity of the actin of muscle to that of a quite different system, the blood platelet, is demonstrated in a study by Booyse, Hoveke and Rafelson (*ibid*, 4083) The molecular weight and sedimentation coefficients of the monomeric G actins are the same, both polymerize to F-actin filaments, and these associate in a characteristic manner with muscle heavy meromyosin, both activating its ATPase, the platelet actin albeit to a lesser extent Structural differences are only apparent in the pattern of peptides generated by chemical cleavage The presence of F-actin filaments has now also been demonstrated in mammalian (HeLa) cells by Schroeder (*Proc natn Acad Sci USA*, **70**, 1688, 1973), in the contractile ring which manifests itself in the final stage of cell division If the cells are extracted at this stage with glycerol, heavy meromyosin can be diffused in, and forms the familiar arrowheads on, the filaments, thus identifying them as F actin If ATP is present this does not occur Other thin threads interspersed between these filaments are conjectured to contain myosin, so that the contractile ring comprises a genuine muscle-like contractile system

A further step towards the unification of muscle and other motion-generating systems has been taken by Oplatka and Tirosh (*Biochim biophys. Acta,* **305**, 684, 1973), who have shown that not only slime mould but also rabbit muscle actomyosin can be made to simulate the cytoplasmic streaming process When sucked, with a supply of ATP, into capillaries, it gives rise under the microscope to all the disagreeable manifestations — those surging tides of mucus—familiar from films of amoebae on the prowl The oscillatory changes in the direction of flow can even be observed, if an ATP regenerating system is included to prolong the activity

HOMOSEXUALITY

Origin of Sexual Drive

from a Correspondent

INTEREST in a disturbance of hormone balance as a cause of homosexuality will be heightened by a report from two workers in California (Margolese and Janiger, *Brit med J*, **3**, 207, 1973) They have shown a significant difference in urinary excretion of male hormones between homo and heterosexual males, but this time using a larger group and aiming at a more accurate psychological assessment than in the earlier work of Margolese published in 1970

The chief male hormone is testosterone which is largely secreted from the testes, but the adrenal gland also secretes a little testosterone, as well as dehydroepiandrosterone, thought to be a testosterone precursor Testosterone is metabolized in the liver to androsterone and etiocholanolone Together with dehydroepiandrosterone these compounds largely make up the complement of 17-ketosteroids excreted in the urine Taken over 24 hours the average excretion of 17-ketosteroids from a normal male adult is about 14 mg, but in the present study the interest centres on the ratio of androsterone to etiocholanolone excretion over periods of 24 h

Sixty-three males were studied, the homosexuals coming from various homosexual organizations such as the Gay Liberation Front and the heterosexuals being drawn from college students Each subject was interviewed by Janiger—a lecturer in psychiatry—and classified using a modified Kinsey sexual inventory into one of six groups from exclusively heterosexual (0–1) through degrees of homosexuality (groups 2, 3 and 4) to predominantly and exclusively homosexual (5 and 6) They were also questioned on their frequency of sexual activity—defined as any activity that resulted in orgasm—and on factors such as parental age and incidence of homosexuality in their families The subjects underwent a physical examination to detect abnormalities in secondary sexual characteristics and the presence of disease

After the exclusion of unhealthy subjects the biochemical studies were done on twenty-three homosexuals, twenty-four heterosexual controls, nine intermediates (Kinsey 2, 3, 4) and one transsexual There was no difference between homo and heterosexuals in physical factors such as genital size or distribution of pubic hair, or in age of parents at the subjects' birth Nor was there any difference in frequency of sexual activity between the two main groups There was, however, a highly significant increase in the incidence of homosexual relatives in the homosexual group

Biochemically, however, although the total urinary ketosteroids did not differ significantly from normal values in the homosexuals or controls, there was a variation in the ratio of androsterone to etiocholanolone For twenty-three of the twenty-four controls the ratio was greater than unity, whereas of the fifteen exclusively homosexual subjects of Kinsey scale 6 in only one case was the ratio greater than unity

As the authors point out, this strengthens support for the hypothesis that the metabolic pathway resulting in high androsterone levels is associated with sexual preference for females by either sex, and that low levels are associated with preference for males by either sex In other words, the view is that a high androsterone level in males is associated with normal sexual behaviour, whereas in females it is associated with homosexual behaviour The opposite situation holds for low androsterone levels

In the past there has been some doubt that the ratios being measured might have been influenced by undetected physical and mental illness in the subjects examined, but the careful physical and psychiatric examination in the present study will have reduced the likelihood of these factors affecting the results

DIAMOND

High-boron Form

from a Correspondent

THE technological uses of diamond are many and include the cutting of hard materials, abrasion, use as a heat-sink, and uses where stability under high temperatures and pressures is required. Theoreticians are also greatly interested in diamond, because it is the simplest analogue of a wide range of technologically-important elements with the same crystalline structure, moreover, the fruits of intensive efforts in theoretical organic chemistry, in which the molecular orbital calculations for carbon–carbon bonds are very advanced, can be passed on for use in the solid-state physics of inorganic materials through this one element

The physics of diamond has been

arduous and slow to develop because of the difficulty of preparing samples in the laboratory and the high concentrations of impurity found in natural diamond, including nitrogen, aluminium, and boron in the parts per million range. The analysis of impurities is, moreover, confused by the presence in most diamonds (both natural and laboratory-grown) of inclusions which may contribute a large proportion of one impurity. One very interesting form of diamond, known as type IIb, is semiconducting. The forbidden gap of diamond is much wider than for its neighbour in group IV, silicon (about 5.7 as against 1.2 eV respectively) and thus the conduction, which is p-type, must derive from impurities. Activation-energy studies showed that the acceptor level lies at 0.35 eV above the valence band but, because of the abundance of impurities present, the impurity producing this level could not be firmly identified. The hypothesis which was best elaborated was that aluminium is the active acceptor impurity. To fit the data, the picture had to be complicated by interaction with other impurities, namely nitrogen which is well established as a deep-lying donor, and with boron, another acceptor of uncertain energy level, which is also known to be present (Dean, Lightowlers and Wight, *Phys. Rev.*, **140**, A352; 1965).

This hypothesis, although fairly widely accepted for a time, was not universally accepted (Wedepohl, *J. Phys. C*, **1**, 1773; 1968) and finally Collins and Williams (*J. Phys. C*, **4**, 1789; 1971) presented the idea, based on more accurate analyses of aluminium in diamond, that boron is a more likely candidate for the dominant impurity. This new proposal was generally accepted by workers in the field, especially because it had the support of some unpublished data of Chrenko, of General Electric Research Laboratories. Chrenko has now released what might be regarded as the largest mass of authoritative data yet available on the subject. He concludes that boron must indeed be the dominant acceptor. General Electric Corporate laboratories are the leaders in the synthesis of diamonds large enough for this kind of research and are one of the few centres in the world where such diamonds with well-controlled amounts of impurity can be synthesized. Writing in *Physical Review* (**B7**, 4560; 1973), Chrenko concludes that there is a good correlation between boron content and acceptor concentration, but aluminium content, intentionally kept low, does not correlate well. What is more, the acceptor concentration is considerably higher than the total aluminium content as determined by neutron activation analysis, thus rather firmly excluding aluminium from contention as the dominant acceptor, although other potential acceptors, for example beryllium, are not as rigorously dealt with.

Considering the previous difficulty in determining boron content (in natural diamonds of the usual experimental size, the total mass present is so low as to be near the limit of detection by any method), the data presented are unique and represent an important new acquisition of knowledge. Chrenko also improves on the moment by reviewing carefully the previous principal hypotheses and thus sets the new data firmly in the framework of the old.

There are, of course, reservations which should be made: the acceptor concentration was estimated from optical absorption rather than by electrical means and the author also admits that the distribution of impurity was not uniform, but showed a reticular pattern. The chief uncertainty in this work is always the unfortunate presence of metal-rich inclusions in many samples, which throws off the calculation of bulk impurity concentrations from bulk analytical data, and caused the original false impression concerning abundance of aluminium. Finally, aluminium has only been demoted, and not eliminated completely as an active acceptor impurity. It is probably true to say, however, that this first report on new, large, high-boron, low-aluminium diamonds gives only a foretaste of the good basic work that can be done when they are more thoroughly studied by a wider range of workers. While it is unlikely that diamonds will be used widely as semiconductor devices, this form of diamond represents a very interesting tool in the study of extrinsic conduction in solids.

RECLAMATION

Changing the Spoil Heap

from our Plant Ecology Correspondent

NATURE is, on the whole, well equipped to cope with calamities, even when they involve the complete destruction of life in an area, for example, following glaciation or volcanic eruption. As soon as the interfering factor is removed, the process of biological succession is initiated in which progressively more complex communities replace one another until eventually a stable climax state is attained. Even most man-made catastrophes are followed by these natural repair processes, but there are certain exceptions which present pressing problems to ecologists concerned with the restoration of over-exploited environments.

One example of a situation in which natural successional processes are inhibited is provided by spoil heaps in which high concentrations of toxic residues remain. There are several reasons why efforts should be made to hasten the process of succession in such situations. In the first place there is the amenity consideration which, although important, is difficult to evaluate objectively. Second, there is the problem of erosion of toxic materials and their redistribution; and, third, there is the possibility of soluble toxins reaching rivers and aquifers from which they might find their way into human tissues. These problems can all be alleviated by encouraging the growth of vegetation on spoil heaps because this will stabilize the material and also reduce run-off water by increasing evapotranspiration.

Breeze now describes (*J. appl. Ecol.*, **10**, 513; 1973) some studies he has made on spoil heaps resulting from chromium extraction processes in the Croal Valley, Lancashire. The reclamation of these waste heaps was proposed by the Lancashire County Council both on the grounds of amenity and in the hope of improving the river Croal. Breeze found that the diversity of algal and macrophyte vegetation of this river is considerably reduced in the region below the spoil heaps.

The waste is the product of various processes, the chief of which was the extraction of chromate salts from chrome iron ore, $FeO.Cr_2O_3$. The ore was roasted with sodium carbonate and lime and the resultant sodium chromate extracted. About 5% of the ore was converted to calcium chromate, however, and as much as 10% of the original ore remained unaltered. Additional waste products included calcium aluminate, calcium hydroxide, magnesium hydroxide and ferric oxide, producing a residue with a *p*H of 12.5. This material was accumulated during the period 1880 to 1968 as spoil heaps up to 15 m high.

The spoil in its present form is eminently unsuitable for plant growth. A reduction in *p*H, however, would increase the solubility and hence the availability of chromium, aluminium and magnesium, all of which are present at toxic concentrations. If the *p*H were reduced to 7, the amount of chromium entering solution would be increased five times.

Breeze has conducted experiments on the toxicity of chromium in its anionic and cationic forms and has found that the chromate anion is toxic at far lower concentrations than the chromic cation. Potassium dichromate is toxic to *Lolium perenne* at 500 mg Cr kg^{-1} soil, whereas chromic sulphate had to be supplied at a level of 5,000 mg Cr kg^{-1} soil to produce equivalent toxicity. Chemical reduction of chromate to chromic ions might therefore alleviate toxicity and permit invasion of the heaps by vegetation.

An alternative technique is to cover

the spoil with a layer of soil. This should be of neutral or alkaline reaction, otherwise its leachate would dissolve more chromium from the underlying spoil. Upward diffusion of chromium would remain a problem; this has been shown to occur through 15 cm layers of soil. An impermeable layer between the spoil and the soil would lead to erosion of the upper soil. It seems, therefore, that chemical reduction of chromate is the best hope for a long-term solution to the problem of reclamation of chromium waste heaps.

EARTHQUAKES

Predicting Locations

from our Geomagnetism Correspondent

EARTHQUAKE prediction must obviously involve both the times and locations of impending events. But having acknowledged that, it is possible to visualize two rather different approaches to the prediction problem with rather different emphases on time and place. It is probably true to say that prediction has most often been perceived as the problem of determining in advance the times of events likely to occur in regions known to be seismic, and in such cases the seismic regions may be regarded as essentially local even though some may have similar characteristics (similar fault types or similar earthquake depth ranges, for example). Thus attempts to predict earthquakes by seeking, for example, premonitory geodetic, geomagnetic or seismic velocity changes have been carried out in specific areas, certainly in the hope that any conclusions emerging may be applicable to other seismic zones, but more realistically in the expectation that the results may be applied at least within the particular region concerned.

Clearly this approach is possible even in the absence of any general framework linking all, or most, seismic zones. Japan, for instance, has long been known to be seismically active, and attempts have been made to predict the times of occurrence of earthquakes since the last century. But the advent of the new global tectonics has opened up a new approach which may be expressed as attempting to deduce, not so much the times of impending events in a particular area, but rather the likely locations of events within a particular time interval. This possibility first became apparent in a general way with the discovery that seismic zones are not randomly scattered about the world but form a series of linked belts now known to correspond to plate boundaries (although some earthquakes also occur outside these belts). At this point it became possible to make a statistical statement to the effect that future events are much more likely to take place along the defined belts than in the interiors of the plates. Moreover, more detailed work on the nature of plate boundaries led to more detailed predictions about where particular types of earthquake would occur—for example, that very large earthquakes are much more likely to occur along subduction zones and along transform faults than along oceanic ridges.

But can this approach be refined? In other words, given that future earthquakes are more likely to occur along the defined belts, can the belts themselves now be subdivided into segments in which the chances of an earthquake occurring during a specified period differ? For although this may not lead to precise prediction in the sense of being able to forecast the exact time and place of a future event, it would nevertheless be of some social importance to be able to predict whether, say, the San Francisco area is very likely or highly unlikely to experience a significant seismic event during the next few decades.

In a long and detailed analysis of the Pacific plate margins, Kelleher *et al.* (*J. Geophys. Res.*, **78**, 2547, 1973) have now shown that it is indeed possible to subdivide the circum-Pacific seismic belt in this way, although they admit that this first systematic attempt is "crude" and that "profound social changes" are therefore not warranted. Their chief aim was to predict the locations of large (magnitude $\geqslant 7$) shallow earthquakes due to take place over the next few decades around the Pacific, and they have done this by successively applying two sets of criteria to give a three-fold classification of marginal segments.

The initial set of criteria was designed to exclude all segments which are not part of a major shallow seismic belt characterized predominantly by thrust or strike slip faulting, and all segments which have ruptured during the past 30 years as a result of large earthquakes. The object of the first of these criteria was largely to remove from consideration those regions not relevant to the principal aim and thus to exclude intermediate and deep earthquakes, large shallow earthquakes within plates and earthquakes associated with normal faulting. Spreading ridges were also eliminated because large shocks rarely occur along them, and a few other areas were removed because of tectonic complexity. The point of the second criterion is that there is now considerable theoretical and observational evidence to suggest that large earthquakes are least likely to occur in the immediate future in zones which have experienced such events in the recent past. In short, there is a tendency for large earthquakes to fill in the "seismic gaps" which have not been subject to rupture for some considerable time. This was first appreciated by Fedotov (*Tr. Inst. Fiz. Zemli Akad. Nauk SSSR*, No. 36, 66, 1965) and was used by him and others to predict earthquake locations in limited areas. Thus Kelleher *et al.* do not claim that their initial criteria are new, although this is the first time they have been systematically applied over such an extended region.

To the areas of "special seismic potential" defined by the initial criteria, Kelleher and his colleagues then applied a supplementary set of three criteria in an attempt to pick out the zones most at risk to large earthquakes during the next few decades. According to the first supplementary criterion, a historical record of one or more large events along a segment is regarded as evidence that similar events can occur there again. If no such record exists, it may be that the strain is being released by aseismic creep or small to moderate earthquakes, and the risk of a large earthquake will be low. On the other hand, it could also be either that the historical record is incomplete or that the recurrence time for large earthquakes is longer than the historical record. This criterion is therefore not foolproof.

The point about the recurrence interval is taken up again in the second criterion, for an area is considered to be particularly at risk in the near future if historical data and relative plate motions suggest that the recurrence time is comparable to the time since the last large earthquake occurred. But although this is straightforward enough in principle, calculated recurrence times are particularly vulnerable to defects in the past record of events and variations in relative plate motions and will thus be subject to large uncertainties. Finally, an area is designated as one of high risk if it appears to be the site of the next event in a series of earthquakes progressing regularly in time and space. There are now several recorded examples of regular progressions of events along extensive sections of plate boundaries, suggesting that many earthquakes are causally related.

By systematically applying the various criteria in detail to each segment of the Pacific belt, Kelleher and his colleagues end up with a map defining three degrees of risk with respect to large shallow earthquakes. The low risk areas are those excluded by the initial set of criteria. The risk in those areas not so excluded is higher, and is higher still in those regions selected by one or more of the supplementary criteria. But as the authors point out, the uncertainties are large. They thus regard their results not as the last word but rather as "working hypotheses to be tested, modified, and discarded if necessary".

LIQUIDS

Water Comes into its Own

from our Molecular Physics Correspondent

THE structural thermodynamics of water, which in the forty years since the classic paper of Bernal and Fowler (*J chem Phys*, **1**, 515, 1933) has so often been a matter of inspired geometrical guessing, shows recent signs of an important fruition which may bring it, if not to the exalted status of the theory of simple liquids, at least to a state in keeping with its general language and methodology Two very substantial articles (Weres and Rice, *J Am chem Soc*, **94**, 8983, 1972, Bell *J Phys C*, **5**, 889, 1972) mark this trend, to which a contributory factor has undoubtedly been the appearance of the first convincing computer simulation of a real water model (Rahman and Stillinger, *J chem Phys*, **55**, 3336, 1971, see also *Nature*, **244**, 256, 1973)

As has been stressed on previous occasions (see *Nature phys Sci*, **230**, 74, 1971) the available evidence on the structure and dynamics of water from both "ordinary" measurements (density, viscosity, calorimetry) and more sophisticated probes (infrared spectra, neutron and X-ray scattering, nuclear magnetic resonance, dielectric relaxation) seems at times as confusing in its variety as equivocal in its implications Moreover, the central feature of any theory of water—the hydrogen-bond—remains lamentably ill-defined and can be expected to be the centre of quantum-chemical controversies for some time to come

Several particular ingredients have combined to make the new models of Weres and Rice and of Bell particularly effective in the present state of knowledge One is the recently improved potential of Ben-Naim and Stillinger (*J chem Phys*, **52**, 5531, 1970) which, following an earlier proposal by Bjerrum, treats the H_2O molecule as a tetrahedron of positive and negative charges supported on a repulsive core Another is the recognition that the lattice-gas model, though somewhat discredited in the theory of simple fluids, comes into its own in the case of water, whose complexity still places it somewhat beyond the reach of the more popular integral-equation methods, such as the Percus–Yevick approach

Given the original Bernal–Fowler picture of an essentially tetrahedral pattern of H-bond linkages, the appropriate lattice cell for the modelling of short-range order is almost unquestionably the partially-occupied body-centred cubic arrangement characteristic of ice-I, within which the H-bonds can "flip" between a well-defined and limited number of configurations, consistent with the so-called "Pauling rules" Although other authors have attempted to explain the temperature-dependence of density in terms of competition with the denser ice-II structure, the computer experiments, at least, seem to rule out this possibility for normal temperatures and pressures

Although both Weres and Rice and Bell share the ice-I lattice as starting point and perform similar analyses of the combinatorial statistics of the water molecules in their lattice positions, their approaches, in fact, diverge considerably Bell, perhaps closer to the spirit of lattice theories, develops his model in terms of two basic parameters, a "bonding-energy" and a "repulsive energy", while Weres and Rice follow through the implications of the BNS potential in great detail, grafting onto their basic lattice model ever more ingeniously-justified elaborations — a quantum harmonic approximation for librational motions, a dielectric continuum to account for inter-cell perturbations, an empirical expansion coefficient to fix the cell dimension, communal entropy taken as proportional to the fraction of intact H-bonds, and so forth, to mention only a few Although at times they come dangerously close to obscuring the wood by the trees, the effect, after some twenty pages, remains a fine balance of cunning and insight, and the results, a handful of figures giving the various contributions to enthalpy and entropy at 0° and 100° C, are no anti-climax Though the Weres–Rice results for H and S are not spectacularly close to experiment, they are, by their own high standards, credible, and, moreover, contain useful subsidiary information, for example as to the importance of quantum contributions to the librational motion Bell, whose approach is overall somewhat less ambitious, rests content that he is able to predict successfully the density maximum, its disappearance at a supercritical pressure, and the observed minimum in isothermal compressibility

Taken in isolation, both these attempts to reach quantitative thermodynamic conclusions might seem open to the charge of squeezing too much out of an unpromising and grossly underdetermined physical situation Both undoubtedly contain an unsatisfactory element of seeming to be "designed" to give the type of results by which the authors set particular store—P-V-T data for Bell, S-H-T data for Weres and Rice, neither seems to offer even the remotest chance of predicting a phase transition without very considerable refinement Nevertheless, an altogether more promising complexion is given to the problem by the Rahman–Stillinger computer simulations which Rice and Weres have gone to some lengths to consider

The "molecular dynamics" approach, though still far short of computing the all-important entropy of the system, nevertheless provides (quite literally) an accurate picture of the short-range order and dynamical correlations which follow from the adoption of a particular potential model Even with the rather restricted samples so far generated (~400 molecules in the most recent work), it now seems clear that several of the wilder guesses as to the nature of the short-range order can be ruled out Thus, although distorted tetrahedral networks of strained H-bonds are a dominant motif, there seem to be no recognizable "clusters" or regions of anomalous density beyond ordinary thermal fluctuations Furthermore, although the bonding system seems reasonably well-defined and "dangling" H-bonds can be seen, there seems to be no separation into "network" and "interstitial" molecules and no evidence of interpenetrating networks of the ice-VII and ice-VIII such as required by some alternative lattice-type theories (see, for example, Perram, *Mol Phys*, **21**, 1077, 1971) Finally, so far as the dynamics can be interpreted, diffusion seems to occur by strongly coupled motions with no evidence of "jumps" from one relatively long-lived configuration to another All this undoubtedly adds up to a picture which, at the short-range level at least, is not too far removed from the severely idealized models which Bell and Weres and Rice adopt

The chief casualty in these findings is, of course, the class of theories whose authors put their faith in the existence of elusive "cooperative effects" in the formation of neighbouring H-bonds, the most picturesque and persuasive of these being the "flickering cluster" model of Frank and Wen (*Discuss Faraday Soc*, **24**, 133, 1957) This and other theories involving substantial concentrations on "non-H-bonded" water have already been under fire from infrared spectroscopists (Stephenson, *J chem Phys*, **69**, 2145, 1965), and their passing will surely cause a sigh of relief from theoreticians who, so far from welcoming the simplicity of the appeal to "co-operative effects", see in their radically N-body character something more like a counsel of despair

Perhaps a large part of the fascination of the water problem lies not so much in its biological importance, or in the judicious rendering of uncertain structural tendencies into soluble mathematics, or in the actual mechanics of what are undeniably tedious calculations —but rather in the exasperating nuances of significance in the process of arriving at what might be called a "best fit" to experimental results drawn from almost every type of physical measurement possible on condensed matter

Embryo Transfer and Sensitivity to Teratogenesis

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This article was submitted at a working party jointly set up by the British Association for the Advancement of Science and *Nature* to study the scientific, legal, political and religious implications of recent advances in biology that increase the possibilities for the control of human development and heredity.

MORE than 80 years ago, Heape[1] recovered two four-cell embryos from one rabbit and placed them in the oviduct of another which had been mated three hours previously. In due course the recipient rabbit (Heape used the term "uterine fostermother") gave birth to six young, four resembling herself and her mate while two had the fur characteristics of the donor rabbit.

Since that time many articles have appeared on the successful outcome of transfer experiments, involving ovarian or freshly ovulated eggs (for fertilization in the recipient or *in vitro*), eggs undergoing fertilization, or cleavage embryos up to the blastocyst stage. In 1971, Adams and Abbott[2] published a bibliography listing 451 original articles on egg and embryo transfer; in addition there were sixteen theses and forty-one books and reviews in which the subject was dealt with. The experimental work involved fourteen different species distributed over six Orders of mammals (rabbit, rat, mouse, hamster, guinea-pig, ferret, mink, sheep, goat, cow, pig, deer, monkey and wallaby). Observations included rates of implantation, birth and foetal mortality, and foetal and neonatal anomaly.

This material represents a considerable body of observation and experience from which two points emerge very clearly. The first is the high frequency of success that can be obtained with egg or embryo transfer in the various animals used. Now that specific requirements are appreciated—in particular that the endocrine status of the recipient be appropriate for the stage of embryo transferred—the establishment of pregnancy and in due course birth of young generally follow. The second point is the rarity of birth defects. Indeed, there does not seem to be a single report in the literature in which any of a great variety of procedures could significantly or even suggestively be linked with increase in incidence of birth defects above the normal level. Prenatal losses certainly occurred, often more frequently than in natural conditions, sometimes they involved late stages of development but they chiefly happened before implantation. Treatments have included (a) fertilization *in vitro* under many different conditions, (b) exposure to culture media of widely varying composition, *p*H and osmolarity, and to environmental temperatures between 0°–40° C for different times, (c) storage of two-cell and eight-cell embryos for many weeks at −269° C, (d) separation requiring development from single cells from two-cell, four-cell and eight-cell embryos; (e) transfer of sheep or cow embryos to rabbit recipients for several days before insertion in a sheep or cow recipient, (f) biopsy of part of the trophoblast in blastocysts; (g) fusion of morulae in pairs or larger aggregates, (h) dissection at the blastocyst stage—bisection to form two blastocysts, exchange of inner cell mass between blastocysts or injection of additional cells from other blastocysts.

The implications of these facts can be brought out more forcibly by looking at some of the research on causes and mechanisms of production of congenital abnormalities. In the course of many investigations attempts have been made to produce birth defects by treating the embryo or the mother during the preimplantation phase of pregnancy. In a few instances positive results have been claimed, but generally the reports are clearly open to other explanations than that involving a direct action on the embryo. For example, Werthermann and Reiniger[3] noted ocular defects in a few rats (about 12%) whose mothers had been subjected to hypoxia in the first week of pregnancy—they could have been due to a detrimental effect on the maternal system. Smith[4] froze female hamsters for 30 to 45 min on different days of pregnancy from 0.5 d to 12.5 d, and killed them just before term. In the litter from an animal treated for 45 min at 2.5 d of gestation all foetuses were "grossly malformed"—none of the other eleven animals frozen in the preimplantation period gave such a result, which could well have been genetically determined. Rugh and Grupp[5] described an increase in exencephaly in the young born to mice irradiated between 0.5 d and 1.5 d after ovulation, but their "control" animals were not examined at the same time, nor sham operated, nor were they known to be comparable genetically, in age or parity; others[6] could not confirm these results with similar treatment. Morriss[7] injected pregnant rats with large doses of vitamin A and examined the litters after birth. In eight young rats, among 144 developing in mothers that had been injected just before the time of implantation (3.5 to 4.5 d after mating), there were malformations of the central nervous system—again probably due to changes in the maternal organism. Lin and Monie[8] reported finding haematomas in three out of thirty-five mouse foetuses developing from blastocysts that had been cultured in 0.5% trypan blue solution or inoculated with a 0.1% solution of this chemical agent, before transfer to recipients. Trypan blue is known to enter blastocysts readily and to persist for many days. Other cases are discussed by Kalter[9].

The remarkable resistance to teratogenesis shown by preimplantation embryos stands in striking contrast to the response that can be elicited from embryos shortly after implantation, during the phase of organogenesis. An impressive range of agents—irradiation, chemical mutagens (including trypan blue), penicillin, aspirin, alcohol, thalidomide, hormones, vitamins A and D, rubella, dietary deficiencies, hypoxia and so on—can produce birth defects, often at a high incidence and even reaching 100%, when applied at this time. The explanation of the difference seems to be essentially simple. The cells of the early cleavage embryo possess in large measure the capacity to form any part or even the whole of the future individual[10], as they have not undergone differentiation and so losses of cells can to some extent be compensated for. The principal effects of teratogenic agents seem to be to kill cells or prevent their multiplication. The effect on the cleavage embryo depends on the number of cells killed or inhibited above a certain proportion, the embryo dies; below that figure, the remaining cells multiply to replace those lost and subsequent development is essentially normal Even with the formation of the blastocyst following its differentiation into two types of cells, some such adjustment is possible because the precise fate of inner-cell-mass cells (from which the new individual develops) is still undecided[11] Shortly after implantation, however, differentiation proceeds apace and cells are set aside for the formation of the various tissues and organs Cell death on any significant scale during organogenesis cannot be made good, and the results are permanent structural and functional defects

A brief word should be said about chromosomal anomalies Inappropriate culture media and the ageing of eggs before fertilization can interfere with egg maturation, the response of the egg to sperm penetration and the cleavage of the fertilized egg, and thus increase the normal incidence of triploidy and tetraploidy in embryos These states are highly lethal, nearly always resulting in early embryonic death, they characterize a large proportion of spontaneous human abortions It is possible for triploid foetuses to survive to birth, and for shortly thereafter, but only as extremely rare events[12,13] In most of these instances survival seemed to have depended on the fact that some tissues comprised diploid cells; the mode of origin of these foetuses is obscure

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Early and Late Methylations in HeLa Cell Ribosome Maturation

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Early and late methylations of HeLa cell rRNA occurring during maturation of the rRNA have been characterized.

KNOWLEDGE[1–5] of the methylated sequences within a mammalian rRNA and its nucleolar precursors is of structural interest, and may help to clarify the role of RNA methylation in mammalian ribosome maturation. We present here an analysis for HeLa cell rRNA

It was thought that all methylation of mammalian rRNA occurs rapidly in the nucleolus on 45S RNA[1–3], but more recent results using HeLa cells[6–8] indicate that at least a few 18S methylations occur later during maturation It is therefore important to distinguish clearly between many early methylations and a few late ones This was achieved in the experiment shown in Fig 1 which demonstrates the late methylation of three 18S products, 30, 34 and 49, absent in T_1 fingerprints of nucleolar RNA[7] One faint, hitherto unnoticed, 28S product (2*a*) is also labelled but no other products are labelled. On the basis of this experiment, and from further comparison of ribosomal with nucleolar methyl fingerprints, we conclude that all other methylations occur early during ribosome formation This early phase of methylation probably commences on nascent 45S RNA[1]

Methylated Oligonucleotides

To characterize the methylated products which arise in T_1 digests of rRNA, we used standard T_1 fingerprints[7] (Figs 1 and 2*a*), and "T_1 plus phosphatase"[9] fingerprints with long separations in both dimensions for resolving uridylate rich products (Fig 2*b*, *c* and *d*).

Sequence analyses were carried out by a combination of procedures using both ^{14}C-methyl-labelled and $^{32}PO_4$-labelled rRNA, after first locating methylated oligonucleotides in ^{32}P fingerprints by a double isotope method The complete sequences of many products were obtained For other products, mainly large ones or those which could not be obtained pure from complex regions of ^{32}P fingerprints, only characterization of methylated components within the oligonucleotides was carried out. Confirmatory identifications were carried out on many products from 32S and 45S RNA Quantification of all products was performed on at least two, and usually three, ^{14}C-methyl fingerprints, made by both T_1, and T_1 plus phosphatase, methods, on each of the four main classes of RNA (18S, 28S, 32S and 45S) The main findings, to be reported in full elsewhere, were as follows (Table 1)

28S RNA contains some seventy-one methyl groups distributed between fifty-four chemically distinct T_1 products Most products are singly methylated and were recovered in molar yields of close to unity (±15%) A few products are multiply methylated, two of the smallest products occur several times per mol, and a very few products occur in clearly fractional molar yields. Of the methyl groups, all except five, which seem to be base methylations, were characterized as 2′-O-ribose substituents. 18S RNA contains some forty-five methyl groups. Most 18S methylated products are different from the 28S products, but a few small products are common to both RNA species[7]. As with 28S RNA, most 18S products were recovered in molar yields close to unity, though there were a few exceptions. Three 18S products contain more than one methyl group (Table 1). One of these is the strong late spot 30 which possesses the sequence, $m_2{}^6Am_2{}^6ACUG$, and is very similar to both a late methylated sequence in yeast 17S RNA[10] and to one near the 3′ end of *Escherichia coli* 16S RNA[11–13]. The two other late 18S methylations are also base methylations but all the early 18S methylations were characterized as ribose methylations, with one possible exception (spot 69) which contains a still unidentified component.

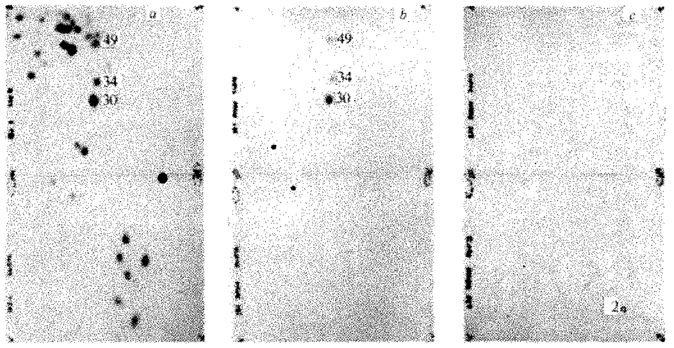

Fig. 1 Late methylations on ribosomal RNA. Two rapidly growing monolayer cultures of HeLa cells, each with 10^8 cells, were incubated with 50 μCi ^{14}C-CH_3-methionine. For controls, Eagle's medium was replaced by 50 ml methionine free medium with 5% dialysed serum, 2×10^{-5} M adenosine and guanosine and 10^{-2} M Na formate[7]. 50 μCi (1 μmol) of ^{14}C-CH_3-methionine was immediately added and the cells were incubated for 90 min. For the other experiments actinomycin D (4 U ml^{-1}) was added immediately after changing the medium, and ^{14}C-CH_3-methionine 5 min later. Cells were collected, cytoplasmic rRNA prepared, and fingerprinted after T_1 digestion as described[7] with one modification—because of the large quantity of RNA required to yield adequate radioactivity after the short labelling period (about 300 μg of 18S RNA and 800 μg of 28S RNA), 'Cellogel' (Reeve Angel) was used instead of cellulose acetate for fractionation in the first dimension of the fingerprints. *a*, 18S control; *b*, 18S with actinomycin; *c*, 28S with actinomycin.

The numbers of methyl groups calculated from this analysis (Table 1) agree well with the numbers recently estimated by a different method, based on the determination of the absolute molar yields of several methylated products in combined T_1 plus pancreatic RNase digests of ^{32}P-labelled RNA[8]. The combined results of these analyses are not consistent with the possibility of extensive duplication of the methylated sequences in HeLa rRNA, as was previously reported for *E. coli* 23S RNA[14]. Nevertheless, the numbers of methyl groups reported here are considerably higher[8] than those estimated previously for HeLa rRNA[3].

A careful comparison was made between rRNA and the precursors, by both T_1, and T_1 plus phosphatase, fingerprints, to test the supposition[3,4] that methylation is confined to the ribosomal sequences of the precursor molecules. There was almost complete correspondence between both the 28S and 32S RNA and the 28+18S and 45S RNA methylation patterns, apart from the absence of known late methylated spots in nucleolar fingerprints. There were a few very minor discrepancies between 45S and rRNA but these seemed to be largely if not entirely attributable to variable incomplete methylation of a few products within 45S RNA. Otherwise the data provide the most direct evidence yet obtained that methylation of 45S RNA is essentially confined to its ribosomal sequences.

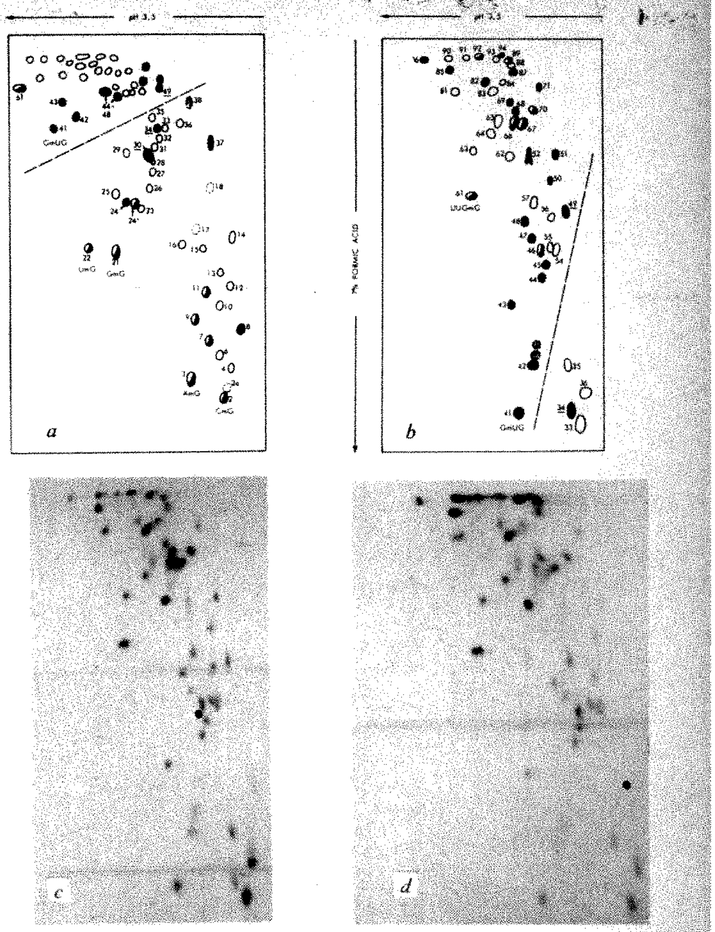

Fig. 2 *a*, Standard T_1 and, *b*, T_1 plus phosphatase keys to CH_3 of HeLa cell rRNA[7], and T_1 plus phosphatase fingerprints, of, *c*, 28+18S and, *d*, 45S RNA. T_1 plus phosphatase fingerprints[9] were made using the following separation conditions. First dimension, cellulose acetate, *p*H 3.5, 4.5 kV for 5–6 h; second dimension, DEAE paper, 7% formic acid, 1.3 kV for 36 h. ○, 28S unique spots; ●, 18S unique spots; ◐, spots common to 28S and 18S RNA. Faint spots are indicated by dotted circles (28S, open; 18S, shaded). Products below the interrupted line were generally fractionated by T_1 fingerprints, those above the line by T_1 plus phosphatase fingerprints. Overlapping 28S and 18S spots do not necessarily signify sequence identity. Several of the smallest products are common to both rRNA species, but several other overlapping 28S and 18S spots yield different products on further degradation. Note the absence of spots 34 and 49 in the 45S fingerprint (spot 30 (2*c*) has run off). The RNA used in these fingerprints was prepared as described previously[7].

Early and Late Methylations

45S RNA thus undergoes rapid methylation in the nucleolus at some 110 points within its ribosomal sequences. Most methylations are on different primary sequences, and all except five or six are ribose methylations.

Later, during maturation, six base methylations occur on 18S RNA, and one very minor one occurs on 28S RNA. Four of the late 18S methylations give rise to the product, $m_2{}^6Am_2{}^6A$.

The large number of different primary sequences which undergo ribose methylation suggests that the specificity for this type of modification resides in secondary structure rather than purely in primary structure within 45S RNA[15,16]. If so, the secondary structures of ribosomal and non-ribosomal sequences must differ substantially from each other, as the latter are not methylated.

That the great majority of methylated products were recovered in molar yields of close to unity (Table 1) suggests

Table 1 Methylated Products in HeLa Cell rRNA

28S	Spot No.	Methylated component (or sequence)	CH_3 groups mol^{-1} RNA Observed	Suggested
Singly ribose methylated products	All except those listed below:			48–49
Multiply methylated and/or base methylated products	2a*	mCG	Faint	0.25 ?
	14	mA; . . AmC or CmA . .	1.60	1.5–2
	28	U(A,mA)CG	0.97	1
	33	mC; C,AAAmU,G	2.22	2
	36	AC$_{3-5}$ GmAAmAG	1.76	2
	62	CmAGmUUG	2.21	2
	63	mUUψAG	1.18	1
	67.28	mC, . . . 2AmU . . .	2.51	~3
	83	. . . UmGmU . . .	1.93	2
	90	. . GmU,UmC,GmAAC . . .	2.53	~3
	92a	. . . . UmGmψ	1.83	2
	93	. . . (A$_2$X)U . . .	1.63	2–3 ?
Sum of 28S CH_3 groups				~71(±1)
Previous estimate[8]				~68
18S				
Singly ribose methylated products	All except those listed below:			35
Multiply methylated and/or base methylated products	30*	$m_2{}^6Am_2{}^6ACUG$	3.67	4
	34*	. . . m6A . . .	0.75	~1
	49*	. . . mG? . .	0.95	1
	68	. . CmA,UmA . .	1.82	2
	85	. . UmC,UmG	2.22	2
Sum of 18S CH_3 groups				~45
Previous estimate[8]				~46

The spots itemized are all unusual in that they contain more than one methyl group and/or a methylated base. Two or more methyl groups exist within a single T_1 product in 28S spots 36, 62, 83, 92a and 93 and 18S spots 30, 68 and 85. For four other 28S spots it is not yet clear whether apparent multiple methylation is due to unresolved mixtures of products. Alkali stable dinucleotides or trinucleotides are underlined, for example, UmC signifies 2′-O-methyl uridylyl cytidylic acid. Product X in spot 93 seems to be a triply methylated tetranucleotide, and is identical to product X of ref. 8. Only the mononucleotide of methylated bases is underlined. Identification of the source of these bases is tentative, but a clear distinction can be drawn between base methylated products and ribose methylated products from alkali digestion and subsequent dephosphorylation. Observed molar yields are based on relative amounts of methyl label in three separate T_1 or T_1 and phosphatase fingerprints. A suggested value of 2 signifies two methyl groups, but only 1 mol of the product for a doubly methylated product (for example spot 62).

* Late methylated products.

a fairly high degree of sequence homogeneity within an animal cell rRNA. This has also been inferred from other lines of evidence[17,18], and is of particular interest in view of the large number of genes which code for rRNA in animal cells[19].

The presence of a late methylated sequence similar to $m_2{}^6Am_2{}^6ACUG$ within the smaller ribosomal subunit of two unrelated organisms, yeast[10] and *E. coli*[11–13], suggests that a similar sequence may be of widespread occurrence and may play some general role. Such a role could be connected with the final stages of maturation of the small subunit, as suggested[11], or with some function during protein synthesis itself, possibly involving a hydrophobic interaction between the small subunit and one of the other components. Methylation of this sequence, however, does not seem to be absolutely essential, at least in *E. coli*, as a viable mutant exists (resistant to the antibiotic kasugamycin), in which the sequence is not methylated[20].

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Mid-plate Tectonics

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There are many examples of mid-plate tectonics which require an explanation. Oceanic island chains, continental graben and rift valleys, and features which pass from continental areas into oceanic parts of the same plate, are particularly important. We argue that these are the result of crustal extension due to tensional stresses — thermal stresses due to the cooling of the lithosphere, membrane stresses due to changes in the radii of curvature or a complicated combination of both.

THE theory of plate tectonics has explained the location and cause of most seismicity, volcanism and active mountain building[1], all of which are associated with plate margins: ocean ridges where plates are created, ocean trenches where plates descend into the mantle, zones of continental collision, and great faults where lateral motion between plates takes place.

There are, however, several striking exceptions where such tectonic activities occur away from plate margins, for example, the Hawaiian Islands where extensive volcanism has created a mountain range near the centre of one of the largest plates. It also seems that the age of volcanism in the Hawaiian chain increases systematically away from the present volcanism. Such "mid-plate" tectonic phenomena can also occur in continental regions, such as the highly active seismic zone centred near New Madrid, Missouri. This seems to be the termination of a belt of seismicity and tectonic activity which extends from eastern Quebec and is associated with the development of the St Lawrence River Valley[2].

Hot Spots and Plumes

Wilson[3] attributed the island volcanicity of Hawaii to the rise of magmas from a nearly stationary "hot spot" in the upper mantle. The motion of the Pacific plate over the magma source resulted in the formation of the island chain. A modification of this theory has been given by McDougall[4].

Morgan[5,6] has further developed the hot spot theory; he identified a large number of apparent hot spots and attributed the magma source to solid state convective plumes rising from the lower mantle. Assuming that the plumes are fixed with respect to the rotational axis of the Earth, he has used the location and age of the island chains to establish the absolute motion of the Pacific plate. The only real test that has been proposed for the hypothesis is a demonstration that the hot spots or plumes are fixed relative to the rotational axis. Morgan[7] found that this could not be done without allowing the plumes to migrate at velocities between 0.5 and 1 cm yr^{-1}. McElhinny[8] has also questioned the validity of the fixed hot spot hypothesis.

Yield and Fracture

An alternative hypothesis for the origin of the Hawaiian chain is a propagating tensional fracture in the lithosphere which causes volcanic activity as it propagates[9–11]. The Hawaiian Islands exhibit tensional features; the shield volcanoes seem to be spaced along en-echelon fractures[12] (Fig. 1*a*). In order to examine this structure in terms of the theory for plastic yielding and fracture of elastic solids we consider the mode of failure of the lithosphere under tension. We assume that brittle fracture will occur near the Earth's surface where the hydrostatic pressure is low but that plastic yielding will occur at depths where the hydrostatic pressure is large compared with the yield stress. The plastic yielding must take place concurrently with the surface fracture to maintain the integrity of the plate. The conditions under which a lithosphere will yield plastically have been derived by Bijlaard[13] (see also Nadai[14]). Assuming that the Mises–Hencky–Huber criterion for yield strength is applicable, Bijlaard showed that a plate under tension would yield plastically at an angle $\beta_y = 35°$ (Fig. 1*b*).

The near-surface pattern of brittle fracture cannot be predicted theoretically. In continental regions there is evidence that the result of a tensional fracture is a graben structure. Studies of the Rhine graben[15] show that the sunken central block is bounded by normal faults with an inclination of 60°–65°. This result is in agreement with the Coulomb–Navier theory for fracture if the coefficient of internal friction is taken to be 0.58 to 0.84.

Clearly the mode of tensional fracture in ocean areas differs from that in continental areas. There is little evidence of graben structures in the Hawaiian Islands. Instead the shield volcanoes seem to lie along en-echelon fractures which have opened and have been filled with magma. The difference may be due to a greater availability of magmas from the asthenosphere in ocean areas. We assume that the oceanic lithosphere fractures under tension in the direction of maximum shear stress, at an angle $\beta_f = 45°$ (Fig. 1*b*). In terms of the Coulomb–Navier theory this corresponds to zero internal friction. When finite deformation takes place these fractures open and fill with magma. The resulting pattern of brittle fractures inclined at 45° and a zone of plastic flow inclined at 35° is similar to the structure of the Hawaiian Islands (Fig. 1*a*). Because the principal trend of the Hawaiian Islands is at 22° to lines of latitude, the predicted direction of the tensional stress is 13° to the west of north and 13° to the east of south.

It is not easy to see how a mantle hot spot or source of magma would result in regular tensional fractures. Localized heating would cause thermal expansion of the lithosphere which would lead to compression. It is possible that shear stresses associated with a plume could operate on the base of the lithosphere but it is not clear how they could produce the observed features. What are the alternative sources for the

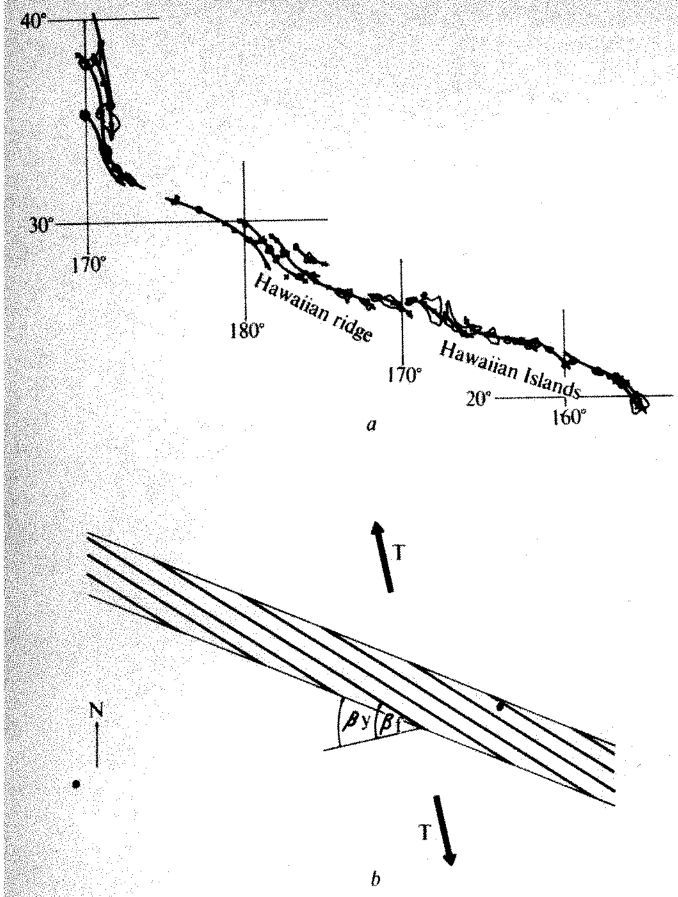

Fig. 1 *a*, Structure of the Hawaiian Islands after Jackson *et al.*[12]. Apparent shield volcanoes (×) seem to lie along en-echelon fractions (——). *b*, Predicted pattern of plastic yielding at an angle $\beta_y = 35°$ and brittle fractures at an angle $\beta_f = 45°$ due to a tensional stress shown by the vectors **T**.

tensional stresses that seem to be responsible for the Hawaiian Islands?

Thermal Stresses

The lithosphere is created in the vicinity of an ocean ridge by the cooling of mantle rock. As the lithosphere convects away from the ridge further cooling takes place and its thickness increases. The lower boundary of the lithosphere can be defined as the isotherm T_y; at temperatures less than T_y there are no significant deformations of the mantle rock on geological time scales at stresses below the yield stress.

An elastic plate which is cooled non-uniformly is subject to thermal stresses. We consider a lithosphere which is cooling as it moves away from an ocean ridge. We take the direction parallel to the ridge axis to be the *y* direction, the direction perpendicular to the ridge axis to be the *x* direction, and the normal to the surface to be the *z* direction as shown in Fig. 2. We assume that deformation in the *y* direction is zero so that the thermal stress is given by[16]

$$(\sigma_{yy})_{th} = \alpha E(T_y - T_0) \qquad (1)$$

where α is the coefficient of thermal expansion, *E* is Young's modulus, and T_0 is the temperature to which the plate is cooled. The resultant stress is a tension parallel to the ridge axis. Taking $\alpha = 3 \times 10^{-5}$ °C^{-1}, $E = 1.7 \times 10^{12}$ dyne cm^{-2}, $T_y = 800°$ C, and $T_0 = 0°$ C as typical properties for a lithosphere we find that $(\sigma_{yy})_{th} = 4 \times 10^{10}$ dyne cm^{-2}. This thermal stress is sufficient to fracture the lithosphere.

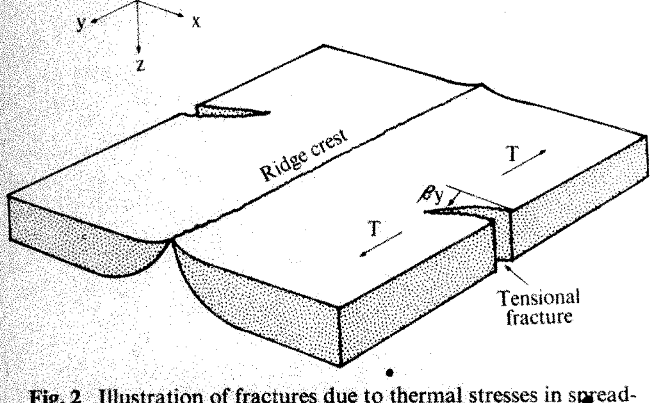

Fig. 2 Illustration of fractures due to thermal stresses in spreading plates. Tensions indicated by vectors **T**.

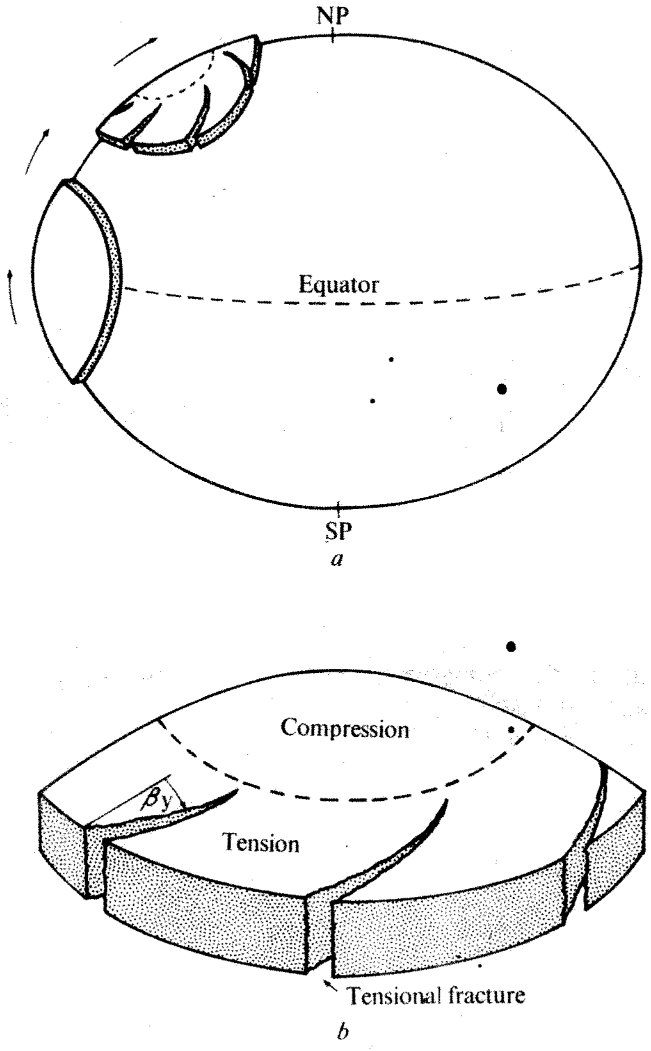

Fig. 3 Illustration of fractures due to non-spherical plate tectonics. *a*, Movement of a plate northwards from the equator showing edge fractures due to an increase in radii of curvature. *b*, Distribution of stresses and fractures due to an increase in radii of curvature in a circular plate.

Thermal stresses due to the cooling of an oceanic lithosphere will be tensions parallel to the ridge where the plate was created. Therefore, the stresses will be aligned with the magnetic anomalies in the ocean floor and will be normal to fracture zones. From the trends of the Murray and Molokai fracture zones and adjacent magnetic anomalies, the direction of the tensional thermal stresses near Hawaii should be 14° west of north and east of south. This is within one degree of the direction predicted in the previous section from the trend of the island chain.

Non-spherical Plate Tectonics

Tensional stresses in a lithosphere may also be caused by membrane stresses due to non-spherical plate tectonics. If the Earth was a perfect sphere the spherical surface plates would be free to move about without deformation. But to a good approximation the Earth is an oblate spheroid with an ellipticity of 0.00335. The principal radii of curvature at the equator are 6,378 and 6,335 km; at the poles the radii of curvature are equal, 6,400 km. If a lithosphere is created on one part of the spheroid it must deform when its latitude changes, for its radii of curvature must change. A plate which is created in the vicinity of the equator must have its radii of curvature increased if the latitude of the plate changes (Fig. 3*a*).

Bending moments are associated with changes in radii of curvature. But for a shell the thickness of which is small compared with its radii of curvature, the stresses associated with bending are small compared with the membrane stresses in the shell. The membrane stresses are simply the result of stretching the plate to different radii of curvature.

According to membrane theory[17] the magnitude of the stresses required to stretch a segment of a shell from one radius of curvature to a slightly different radius of curvature is given by

$$\sigma_{\mathrm{M}} = C_1 E \, \Delta R/R \qquad (2)$$

where R is the initial radius of curvature, ΔR is the change of radius of curvature, and C_1 is a constant of order 1. If the radius of curvature of a circular segment of a spherical shell is increased, the edge of the shell will experience a tangential tensional stress and the centre of the shell will be in compression (Fig. 3*b*).

Assuming that ΔR is the difference between the radii of curvature at two locations on the Earth the ratio $\Delta R/R$ is related to the ellipticity of the Earth ε by

$$\Delta R/R = C_2 \varepsilon \qquad (3)$$

where C_2 is a function of the difference in latitude between the two points on the Earth. If this difference is a significant fraction of 90° then the constant C_2 will be of order 1. Combining equations (2) and (3) gives

$$\sigma_{\mathrm{M}} = C_1 C_2 E \varepsilon \qquad (4)$$

With $\varepsilon = 0.00335$, $E = 1.7 \times 10^{12}$ dyne cm^{-2}, and setting $C_1 C_2 = 1$ we find that $\sigma_{\mathrm{M}} = 5.7 \times 10^9$ dyne cm^{-2}. The membrane stresses due to the movement of the lithosphere over the surface of the non-spherical Earth are sufficient to fracture the lithosphere.

Fractures due to membrane stresses would be expected to appear in mid-latitudes because the change in the radii of curvature of the Earth with latitude is a maximum at a latitude of 45°. The point of generation of such fractures would be nearly fixed in latitude. For northward moving plates in the northern hemisphere such as the Pacific plate and the Americas plate the crack should be propagating southwards. This is the case for both the Hawaiian Islands and the New Madrid, Missouri–St Lawrence Valley tectonic zone.

Non-spherical plate tectonics requires a finite extension to relieve the membrane stresses. This is observed in rift valleys and graben structures. The Rhine graben has a mean width of 36 km and the extension across the valley is estimated to be 4.8 km (ref. 15). Other rift and graben structures have widths and crustal extensions of the same order. Burke *et al.*[18] associate the Rhine graben with a hot spot. It is, however, not clear how a hot spot or plume could lead to the known unidirectional crustal extension across the Rhine Valley. Non-spherical plate tectonics provides an explanation for a permanent extension of the crust of this magnitude.

There may be further implications of both thermal stresses and membrane stresses. For example, the fractures caused by these stresses may initiate the breakup of continents, for example, for the formation of the Atlantic Ocean. Also, the additional force required to change the latitude of a plate due to the membrane stresses would favour east–west seafloor spreading over north–south seafloor spreading.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Subsidence of the Venice Area, during the Past 40,000 yr

THE present day subsidence of the Quaternary deposits of the plain of Venice can be considered to be the result of either geological factors—the plain is situated on the northern margin of the subsident area of the Po valley—or of human activity over several centuries, such as overexploitation in the confined aquifers of low turnover[1], urban and industrial development on unconsolidated sediments.

The respective contribution of the different factors affecting subsidence may vary from place to place. Drillings, continuous corings[2,3] and seismic profiles[4] can provide average sedimentation rates of about 0.5 to 1.0 mm yr^{-1} since the Upper Pliocene from north to south of the lagoon of Venice. Geodesic studies[5], available since the early 1900s, have shown that in some places, Lido di Venezia for instance, the soil is now sinking at a velocity close to 8 mm yr^{-1}.

In order to study the geological component of subsidence at an intermediary time scale, systematic analysis of the chronology of the upper Quaternary deposits has been undertaken using ^{14}C measurements. This study is designed to determine whether or not "geological" subsidence for the past 40,000 yr

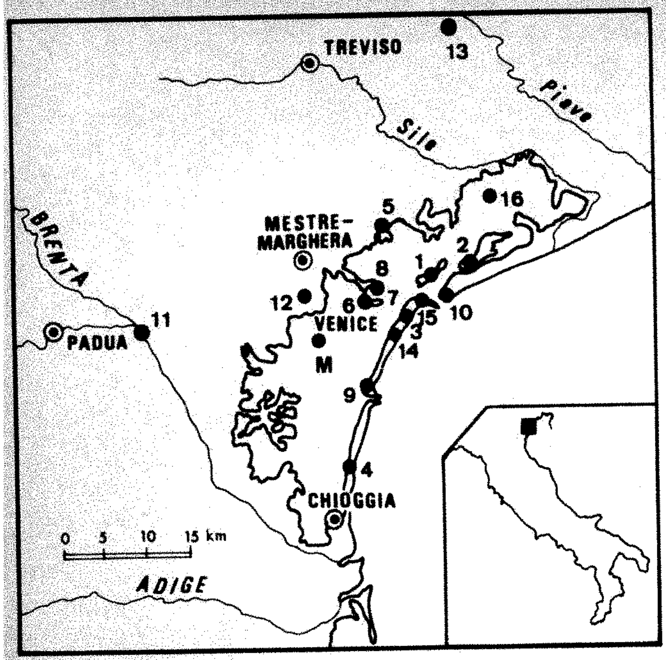

Fig. 1 Location of samples. 1, Sant' Erasmo; 2, Treporti; 3, Lido of Venice San Nicolo; 4, Lido di Pellestrina; 5, Cà Montiron; 6, Venice Drilling CNR I; 7, Venice civil hospital; 8, Venice civil arsenal; 9, Alberoni; 10, Punta Sabbioni; 11, Alveo Brenta; 12, Conca Romea; 13, Candelù; 14 and 15, Lido of Venice; 16, Canale Cenesa; M, Motte di Volpego[9,14,15].

has been constant. If the subsidence has varied, has there been an acceleration in recent times?

The samples studied consisted of peats and peaty muds, vegetal relicts, shells, and carbonates. All of the samples were collected as cores whose locations are given in Fig. 1. The ^{14}C measurements were performed by liquid scintillation after synthesis of benzene[6]. No correction was applied to the apparent ages.

Peats located throughout the area give a regular pattern when we plot depth against present soil surface (Fig. 2*a*). The correlation is somewhat better if related to the average sea level (Fig. 2*b*), except for the samples from inland (samples 11 and 13). From about 40,000 to 22,000 yr BP the correlation between age and depth is linear. The slope is about 1.2 mm yr^{-1}. Between 22,000 and 18,000 yr BP a very high sedimentation rate produced at least 17 m of deposits. The basin has not given any more continental document since 18,000 yr BP, but the total thickness of this deposit may have been greater because it is terminated by an unconformity.

The information derived from the marine shells is very different. None is older than 5,900 yr, although they are at times located at depths greater than peats which laterally are much older. The shelly deposits can reach more than 20 m for the past 5,900 yr. In a plot of depth against age there is no general correlation. Further, measurements on shells from a single core do not show linear age-depth relations but give rough curves showing that the rate of marine deposition has decreased between 5,900 and 2,020 yr BP. The accumulation rate is greater than that which could be attributed to the Flandrian transgression (Fig. 2*b*).

The radiometric results lead to the following sequence of geological events.

(1) Continental sedimentation. Peats and interbedded fine-grained terrigenous sediments are thought to represent repeated fluvio-lacustrine cycles. The regularity of the apparent ages given by peats coming from different locations which are widely spaced suggests that sedimentation took place in a basin isolated from the sea at a constant rate of accumulation which

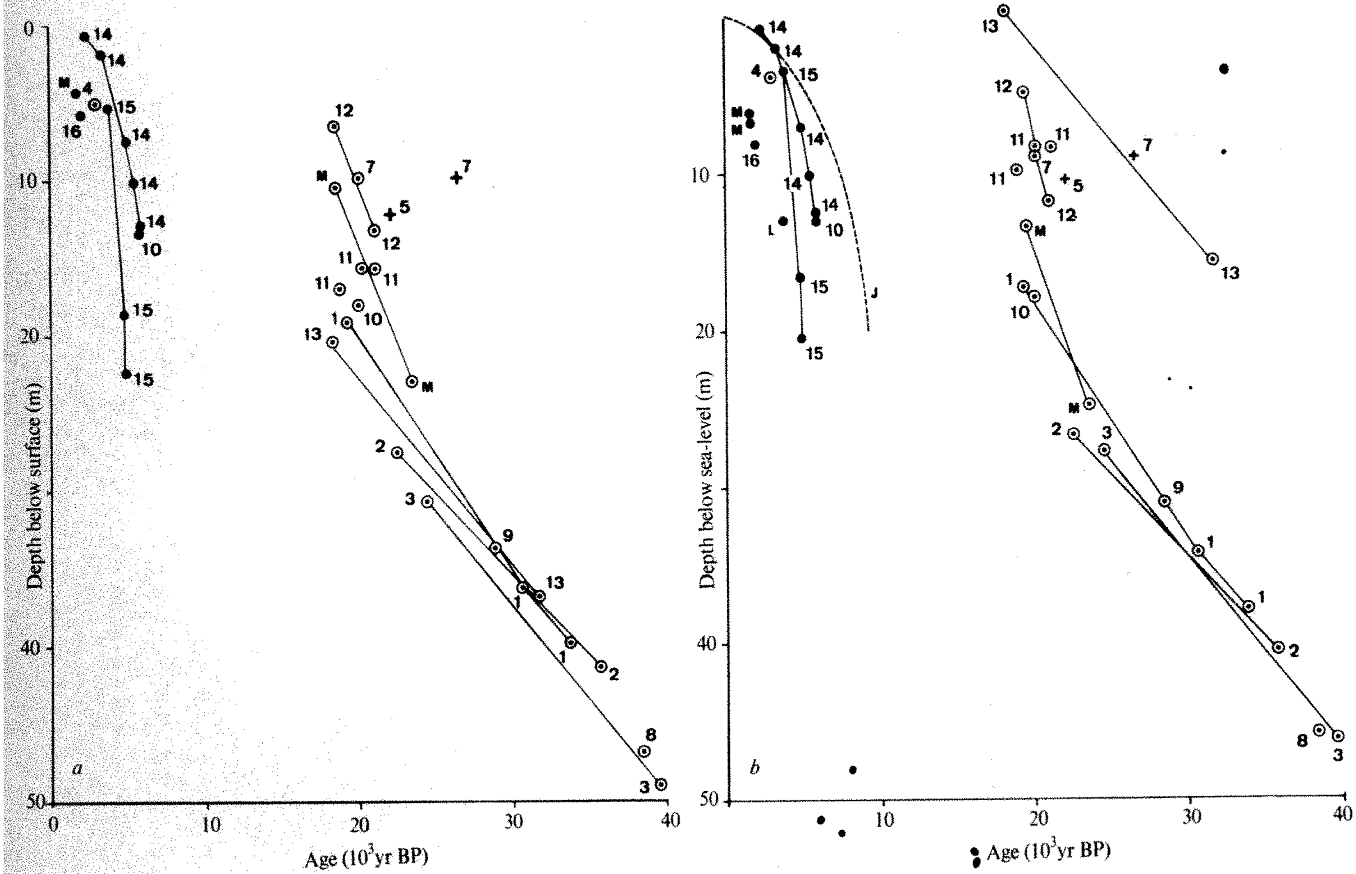

Fig. 2 Age/depth relation. *a*, Relative to ground level; *b*, relative to present sea level. Locations as Fig. 1. ○, Peats; ●, marine shells; +, limy fraction of the sediment suspected of containing reworked carbonate. Peat of location 4 (Lido di Pellestrina) must be related to a stage of Flandrian transgression. We note that for continental deposits the correlation between age and depth is generally better if plotted using present sea level except for the samples coming from the inland (Candelù: location 13). During the Holocene, the accumulation rate is greater than the general Flandrian transgression rate as indicated by curve J (ref. 13) for the Netherlands. Previous radiometric data were obtained on core at Motte di Volpego[14] (M) and on the immersed beach rock at Lignano, 80 km NE of Venice[16] (L).

was essentially controlled by the subsidence for the interval 40,000 to 22,000 yr BP. The average rate (1.2 mm yr^{-1}) seems greater than that (0.5 to 1.0 mm yr^{-1}) determined by seismic methods in the Venice area[4]. The deposits remain continental in character between 40,000 and 30,000 yr BP which is an epoch of relatively high sea level in the eastern Mediterranean[7]. The basin was not invaded and, assuming a minimum value of 1.2 mm yr^{-1} for subsidence, it seems that the basin was at least 10 to 15 m above sea level at that time.

The drastic increase in sedimentation from 22,000 to 18,000 yr BP can be attributed to an increase of water supply (and sediments) due to an increase in the pluviosity and to a sudden increase in local or regional continental subsidence.

This period of 22,000 to 18,000 yr BP covers the glaciation maximum which is generally correlated with a pluvial epoch. But in this area the fluvial supply is considered low because of the water retention in the Alpine glaciers[8] as indicated further by palynological data which suggest a rather dry climate[9] in the area.

Although the development of the alpine glaciers during the last Wurmian episode was probably very extensive[10], we cannot demonstrate any epirogenic effect which would have effected an overcharge of ice on the continent, but a tectonic effect is highly probable in the next period (between 18,000 and 5,900 yr BP). It could have begun at about 22,000 yr BP.

Whatever the reason, the accumulation of sediment during this period was at least 5 mm yr^{-1}.

(2) Continental emersion. Between the last continental deposits dated in the area and the earliest marine accumulation recorded in the cores, there is an interval of about 12,000 yr (approximately 18,000 to 6,000 yr BP). Because of the possible effect of post-depositional erosion during this period, the value for the break is a maximum. During this time the balance deposition-erosion was equal to zero or negative. It probably occurs as a general decrease of the level of the aquifers correlated with the epoch of lowest sea level[11]. The shallower argillaceous deposits of the previous episode are compacted and oxidized[12] and give an indurated level, the so-called "caranto", the most stable layer for foundation works in the area. This level is representative of the limit Pleistocene-Holocene.

The results from Candelù suggest that the whole area was tilted by an upward movement on the continent and probably a downward movement toward the Adriatic basin. This movement is indicated by the shift of the representative points (No. 13) if we plot apparent age against present sea level instead of against group surface (Fig. 2*b*).

(3) Marine transgression. Several factors (variations in initial ^{14}C content of dissolved carbon in brackish ambients, accumulation of organisms either as biocoenosis or as thanatocoenosis, variable thickness of water at the moment of deposition) can lead to non-consistent values in the relationship between radiometric ages and sea levels. Nevertheless, certain statements can be made. The sea came into the basin at about 6,000 yr BP with the Flandrian transgression. It was the first marine incursion in the basin since before 40,000 yr BP and probably since, at least, the neothyrrenian (Ouljian) transgression at about 80,000 yr BP (ref. 11). The Flandrian transgression reached a maximum after 2,000 yr BP as shown by the age at the upper part of the Lido island in the lagoon. The sea covered a relief of deep channels (at least 20 m in the north of Lido island, location 15 on Fig. 1) of tidal origin or those individualized earlier by river erosion. The deposition of shells then took place in these channels very rapidly at the beginning of the transgression and then more slowly. The poor correspondence for the combined data between age and depth for the shell material is probably due to the control of their accumulation rate by the size and biotic activity in the respective channels. All the representative points in the age/depth diagram lie under the curve established for the Netherlands[13]. This means that the accumulation rate of marine deposits was greater than the rate of Flandrian transgression. Hence the subsidence was still going on, although attenuating because the upper points at about 3,000 yr BP are very close to the general curve. So the beginning of the human settlement in the area seems to coincide with a period of ground stability.

These conclusions are in good agreement with the few data already obtained on the vertical profile in Motte di Volpego[9,14,15]. But the concept of a continuous fluviatile and lacustrine sedimentation, from about 25,000 yr BP to 2,000 yr BP (Fig. 24 in ref. 14), is no longer compatible with the results obtained.

The palaeogeographical evolution of the area can be summarized as follows: continuous subsidence in a marshy continental basin with approximately the same rate of accumulation for sediments and peats (from 40,000 yr BP and before, until 22,000 yr BP, this rate is about 1.2 mm yr^{-1}); drastic increase in the same kind of accumulation up to 5 mm yr^{-1} and maybe more in the same basin between 22,000 yr BP and at least 18,000 yr BP as a very probable consequence of tectonics (emersion stage with induration of the superficial levels at the end of the episode); marine transgression since about 6,000 yr BP in channels of erosion, and then in the whole area, accompanied by high rate of accumulation.

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Evolution of Triple Junctions

THE boundaries between the rigid plates which make up the Earth's crust are recognized as being of three distinct kinds: ridges, from which new crustal material spreads symmetrically; trenches, at which plates descend back into the mantle; transform faults, along which plates may slip relative to each other[1-5]. An important concept is the triple junction[6], which is the point at which three plate boundaries meet. Discussions of the development of oceanic and continental crustal features almost inevitably contain considerations of motion, stability and instability of triple junctions. McKenzie and Morgan[6] showed there are sixteen possible triple junctions and set out rules for examining their stability. They concluded that fourteen of them were stable under certain conditions. Here I point out that fifteen of the triple junctions are stable in the appropriate conditions.

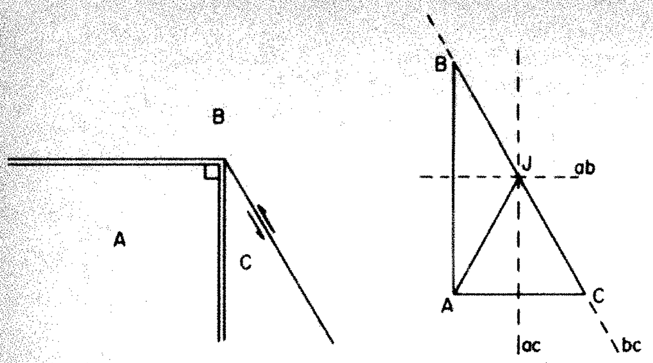

Fig. 1 Example of a stable RRF triple junction along with its velocity triangle. The two ridges meet at right angles. J is the representative point of the triple junction.

In what follows R, T and F stand for ridge, trench and fault, respectively. I assume that at a ridge, spreading occurs at right angles to the strike of the ridge, and that lithosphere is consumed only from one side at a trench.

I consider the ridge-ridge-fault triple junction (RRF) which McKenzie and Morgan stated is unstable. I will show that such junctions can be constructed which are stable if the two ridge elements meet at right angles as in Fig. 1. The condition that the three plates A, B and C be in rigid body relative motion is that the relative velocity vectors for the plates should form a triangle. In Fig. 1 I show the appropriate velocity triangle. As McKenzie and Morgan pointed out, there are, however, additional conditions required for triple junction stability. That is, one must find, in the velocity space in which the triangle is drawn, a point representing the relative velocity of a reference frame in which the triple junction is stationary. If such a point exists, the triple junction is stable. This point is found in Fig. 1, using the procedure of McKenzie and Morgan. Thus an observer moving with uniform velocity along ridge AB (the ridge dividing A from B) would have his motion represented by a point on the perpendicular bisector (ab) of side AB of the triangle. If this observer were actually fixed relative to the ridge, his representative point would be at the midpoint of AB. Similarly, an observer moving along ridge AC with uniform velocity would have a representative point in velocity space on the perpendicular bisector (ac) of the side AC. An observer moving along the transform fault CB with uniform velocity would have a representative point somewhere on bc which is a straight line encompassing side BC and its extensions in both directions. Now these three lines, ab, ac and bc, meet at a point (Fig. 1), so an observer moving with a velocity represented by this intersection point would be able to remain above both ridges and the fault simultaneously, which is only possible at the triple junction. Therefore, there does exist a reference frame in which the triple junction is stationary and the RRF arrangement of Fig. 1 is stable, which completes the proof. The velocity of this particular reference frame with respect to plate A is clearly given in magnitude and direction by the line AJ in Fig. 1.

I note that only when the two ridge elements are orthogonal is the RRF triple junction stable. This is because only then do the two perpendicular bisectors ab and ac intersect on bc. The particular case drawn by McKenzie and Morgan has the two ridges forming a continuous straight line with the fault lying perpendicular to this line. This is an unstable junction, as they note, but as I have just shown, their general conclusion that all RRF triple junctions are unstable is not correct.

Finally, I point out that the point J in velocity space giving the velocity with which the ridge-ridge-ridge (RRR) triple junction moves is the circumcentre of the appropriate velocity triangle and not in general the centroid as stated in the original paper[6]; and the stability condition for the ridge-ridge-trench (RRT) triple junction given by McKenzie and Morgan should be changed to read "ab must go through the circumcentre of ABC".

I thank Professor G. D. Garland for discussions.

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Latitudinal Extent of Late Precambrian Glaciations

LATE Precambrian glaciations are widely recognized to have been extensively distributed (see, for example, ref. 1) but there are few quantitative data to show whether they reached low latitudes. If this can be demonstrated it will be legitimate to regard Late Precambrian tillites as stratigraphic marker horizons[2].

Geochronological studies of recent years have given some absolute control of the age of many of the tillite occurrences. According to Dunn *et al.*[2] the Egan-Morinoan Glaciation of Australia is 670 m.y. old and the Moonlight Valley–Sturtian Glaciation is 750 m.y. old. A time span of 675–560 m.y. is given[3] for the Vendian of the USSR, and Pringle[4] concludes that the Varanger Ice Age of northern Norway occurred at about 668±23 m.y. Stratigraphically controlled ages define the intervals of late Precambrian glaciation in Africa. The Grand Conglomérat of Zaire was deposited both as a tillite and a fluvio-glacial deposit and has a maximum probable age of 950 m.y. (ref. 5). The Petit Conglomérat was deposited between two early phases of the Katangan orogeny dated at 710 m.y. and 670 m.y. BP (ref. 5). Schemerhorn and Stainton[6] equate the Lower and Upper "tilloids" of the West Congo System in west-central Africa with the Grand and Petit Conglomérats. Tillites of probable similar age are found in Ghana, Togo, Dahomey, the western Sahara and the Anti-Atlas of Morocco, and a possible late Precambrian tillite is found in Sierra Leone and Guinea[7].

In the Orange River area of south-western Africa, Kröner[8] found cold water rudites and signs of fluvio-glacial sedimentation in the Upper Hilda Formation of the Gariep Group. These may correlate with the Bushmannslippe glacial sediments overlying the Nosib Formation further north and have a maximum age of 719±28 m.y. Also the lower part of the Gariep Group deposited at <850 m.y. indicates a wet and cold climate during deposition. These tillites predate those found in the Nama Group and the Damara Group (with which the Nama is now correlated[8]). The Nama Group has a maximum age of 653±70 m.y. and the topmost member is probably Lower Cambrian. These younger Infra-Cambrian glacial horizons occur in close association with sediments seemingly deposited under warm conditions in low latitudes. The Portaskaig Boulder Bed of the Scottish Dalradian, interpreted as a subaqueous tillite[9], occurs with limestones, dolomites, algal stromatolites and possible sun-cracked quartzites[10] in a similar setting. A sparse amount of palaeomagnetic data from rocks associated with the glacial deposits of Spitzbergen and Southern Norway suggests that they lay in low latitudes during formation.

A widespread extent for Late Precambrian glaciations has been disputed from analogies with Phanerozoic situations[11] and scepticism about the nature of some tillites[12,13]. Most of the evidence, however, leave no doubt that most of the described formations are tillites[7], and sufficient palaeomagnetic data are now available to examine the palaeolatitudinal distribution of many occurrences. The poles from Africa spanning the interval during which the Late Precambrian glaciations took place are listed in Table 1, and the north poles are plotted on a stereographic projection in Fig. 1. Africa lay in low latitudes from before 1,000 m.y. until post-Lower Cambrian times, and all results obtained from Africa for the interval 740 m.y. to the Lower Cambrian give pole positions close to the present pole showing that Africa occupied a position close to its present one with respect to the poles for a "quasi-static" interval occupying this period. Analysis of palaeosecular variation[20] and the agreement of palaeomagnetic results over large areas of Precambrian shield[21,22] imply that the geocentric dipole model for the behaviour of the Earth's magnetic field is applicable to at least the latter part of Precambrian time. It is therefore legitimate to draw conclusions concerning the geographic poles from the palaeomagnetic results, and the available data furthermore allow Africa to be considered as an integral continent before the "Pan African" orogeny (600±150 m.y., ref. 14 and my unpublished work with J. C. Briden and K. Lomax).

Localities of Late Precambrian tillites occur throughout the length of Africa[7] and from the palaeomagnetic data I conclude that they straddle the palaeoequator of the time. The tillite localities of Australia also appear to have lain within 30° of the equator of the time, but it is impossible to be certain of this from the available palaeomagnetic data. The older Precambrian palaeomagnetic poles from Australian haematite ores[23] and dated igneous rocks[21] suggest that a reconstruction similar to that of Carey[24] was applicable to the Proterozoic, although two new Late Precambrian or Lower Cambrian results from Australia[25] do not agree with the African results using this reconstruction. Within Africa a very large polar shift in excess of 90° is identified in the Lower Cambrian from the difference between poles 7 to 12 in Fig. 1 and poles 15 to 18. This is the largest single polar shift yet identified in geologic time but is confirmed by South American data[26] after correction for Phanerozoic drift (Fig. 1) and may include poles 13 and 14 (Table 1) from Africa. This polar shift does not affect the conclusion that the Late Precambrian tillites of Africa were deposited in low latitudes because it postdates the age of these occurrences. The Fish River Formation pole (No. 12) at the start of the shift lies above the tillite horizons of the Nama Group and is probably basal Cambrian in age[27].

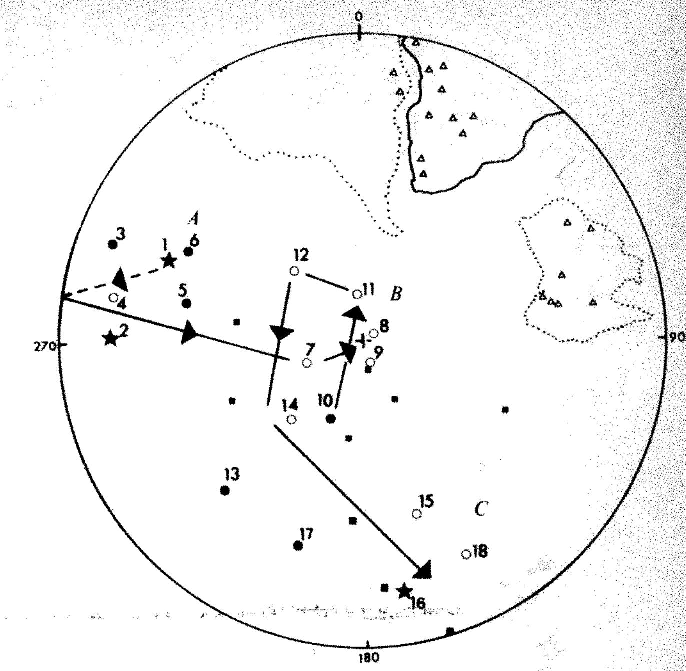

Fig. 1 Palaeomagnetic north poles from Africa for the interval 900 to 500 m.y. plotted on a stereographic projection. The poles are listed in Table 1; closed symbols refer to poles, open symbols to antipoles and stars to pole on the back hemisphere of the projection. The arrowed full line shows the probable migration path of the north pole relative to Africa, the squares are poles of Thompson[26] attributed to the Cambrian after correction for Phanerozoic drift. The dotted outline of Australia is the pre-Mesozoic reconstructed position after Cary's[24] reconstruction and the triangular symbols refer to Late Precambrian tillite occurrences listed by Harland[1]. *A*, Mostly pre-glacial poles; *B*, poles for glacial interval; *C*, post-glacial.

Unfortunately the Late Precambrian palaeomagnetic data from North America are sparse, but the apparent polar wander curve of Irving and Park[22] places North America entirely between palaeolatitudes of ±20° during the interval 800–600 m.y. BP and implies that the North American Late Precambrian tillites were also formed in low latitudes.

Table 1 Palaeomagnetic Poles from Africa Belonging to the Interval 900 to 500 m.y.

Pole No.	Rock unit and locality	Age (m.y.)	Pole position °E	Pole position °N	Reference
1	Dykes, Klein Karas, South West Africa	878±41	294	+20	14
2	Kigonero Flags, Tanzania	>890	273	+11	15
3	Malagarasi Sandstone, Tanzania		292	−7	15
4	Bukoban intrusives, Tanzania	806±30	101	+11	15
5	Gagwe Amygdaloidal Lavas, Tanzania	813±30	283	−29	15
6	Manyovu Red Beds, Tanzania	<813±30	298	−24	15
7	Mbozi Complex, Tanzania	743±30	68	+72	14
8	Pre-Nama dykes, South West Africa	653±70	228	+85	14
9	Sabaloka Ring Structure, Sudan	>540	339	+83	16
10	Plateau Series, Zambia (i)		205	−60	14
11	Plateau Series, Zambia (ii)		173	+71	14
12	Fish River Formation, Nama Group, South West Africa	Lower Cambrian	137	+53	14
13	Doornpoort Formation, South West Africa	Remagnetized by Katangan folding (580 to 680 m.y.)	225	−22	14
14	Lavas, Morocco	"Middle Cambrian"	34	+53	19
15	Ntonya Ring Structure, Malawi	630±24	345	+28	17
16	Plateau Series, Zambia (iii)	Lower Palaeozoic	172	+10	14
17	Plateau Series, Zambia (iv)	Lower Palaeozoic	199	−21	14
18	Hook intrusives, Zambia	500±17	336	+14	18

Poles are listed in probable order of age. See references for discussion of quality and age control of the pole positions.

An impressive relationship has been demonstrated in Africa for the Palaeozoic between the incidence of continental glaciation and polar movements. Lower Palaeozoic poles[28] agree with the evidence of continental glaciation in north west Africa during Ordovician and early Silurian times, and the shift of the south pole to its Upper Palaeozoic position near southern Africa correlates with the evidence for glaciation here[29]. This incidence of glaciation with polar movement is not observed in the Late Precambrian, and I conclude that there was a large contraction in the scale and areal extent of glaciation close to the base of the Cambrian. Possible implications of this phenomenon have been discussed elsewhere[30].

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Primordial Rare Gases in the Deep Earth

I HAVE suggested[1] that mantle-ambient rare gases are to be found in deep-sea basalts, trapped there by the same mechanism responsible for trapping excess ^{40}Ar. A previous search in such basalts dredged from an East Pacific seamount revealed gases similar to atmospheric in both elemental and isotopic ratios[2]. I report here analyses of three Atlantic Ocean basalts whose elemental rare gas ratios are distinctly different from atmospheric, and which approximate primordial rare gases as seen in meteorites and the lunar surface.

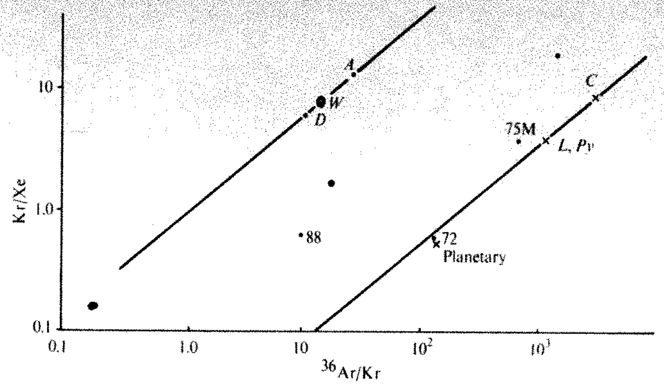

Fig. 1 Kr/Xe as a function of ^{36}Ar/Kr. The points *A*, *W*, *D* (defined in the text) define the values to be expected in a rock which samples the terrestrial atmosphere. The values *C*, *L*, *Py*, and Planetary define the values to be expected in a rock which samples primordial gases.

The basalts studied here were dredged from along the Vema Fracture Zone, close to the Mid-Atlantic ridge. Samples 88 and 72 are glass rims, sample 75 M is an interior specimen. They will be described in detail elsewhere. Fission track ages and K/Ar ages on related rocks are consistent with their having erupted on the active ridge. Initial rare gas studies showed that these particular rocks contain large amounts of excess radiogenic ^{4}He and ^{40}Ar, so they were expected also to have trapped the mantle-ambient non-radiogenic rare gases. Approximately 1 g chunks of whole rock were analysed. The data are presented in Table 1 and Figs 1 and 2.

The previous study[2] demonstrated that rare gases sorbed from an atmosphere-like reservoir will have Kr/Xe/*vs* ^{36}Ar/Kr lying along a straight line on a log-log plot, as in Fig. 1. Here *A* is the atmospheric point, *W* represents several data on atmospheric rare gases dissolved in water, and *D* represents atmospheric gases adsorbed on the surface of wind-borne dust grains. Several data from the East Pacific seamount reported previously all lie along the line drawn through these three points. By contrast the primordial rare gases are shown by the point *C*, which represents cosmic abundances estimated by Cameron[3]; the point *L*, *Py* represents data obtained on lunar fine material[4] and the meteorite Pesyanoe[5] and constitutes the best available experimental approximation to solar wind gases. The point Planetary represents the so-called planetary component of the primordial rare gases[6]. The line through these points is parallel to the atmospheric line, implying a similar relationship between the planetary and solar components of the primordial rare gases.

Gases sorbed from an atmosphere-like reservoir of rare gases should lie along the upper line, as did those from the Pacific seamount and subaerial basalts; gases sorbed from a primordial-like reservoir should lie along the lower line, as do those from meteorites[2]. Gases containing a mixture of the two components should lie in the area between the two lines. The data from the Atlantic Ocean rocks are labelled 88, 72 and 75 M.

The data clearly show large contributions from a non-atmospheric, primordial rare gas reservoir, most likely constituting the mantle region sampled by the magmas which have resulted in these rocks. The absolute amounts of these gases are shown in Table 1, as are meteoritic data. I note that in a rising magma the rare gases should be relatively enriched in the erupting material, so that the measured concentrations are an upper limit to the actual magmatic concentrations.

The ^{4}He concentration is mostly radiogenic, resulting from the decay of U and Th before eruption. Therefore the measured ^{4}He is only an upper limit to the primordial component. The Ne content was masked by high background levels, and so only upper limits were measured. These limits for ^{4}He and Ne are distinctly below normalized solar or cosmic abundances

Table 1 Rare Gas Abundances in Atlantic Ocean Basalts

Sample	^{4}He	Ne	^{40}Ar	^{36}Ar	Kr	Xe
75 M	780	< 1.5	1.850	20.5	0.031	0.0080
72	19.8 × 10^4	< 1.9	7,000	1.67	0.013	0.023
88	24 × 10^4	< 30	33 × 10^4	3.75	0.38	0.62
Meteoritic planetary	~ 25 × 10^4	5–100	—	10^2–10^3	1–100	1–300
Meteoritic solar	~ 10^7	10^4–10^5	—	10^3–10^4	5	~ 1

Ne, Kr, and Xe are given as total elemental abundances. Absolute abundances are accurate to ~ ±20%, except for Ar ~ ±5%. All data in units of 10^{-10} s.c.c. g^{-1}.

(Fig. 2) but cannot be distinguished from atmospheric or planetary values (except that the Ne in sample 75 M is distinctly below atmospheric). If the magmatic rare gas reservoir is solar or cosmic in character, it has strongly degassed its He and Ne while retaining the heavier rare gases.

Isotopic data are not as precise as one would wish due to the small sample sizes necessary for complete cleanup and to minor nonlinearities in the recording equipment. At present I can specify that all isotopic ratios are within ±5% of atmospheric. This accuracy is not sufficient to distinguish between atmospheric and primordial components, with the exception of ^{129}Xe which might be expected to show a large overabundance due to *in situ* decay of the extinct nuclide ^{129}I. No such anomaly was found.

The previous study[2] showed the rare gases trapped in an East Pacific seamount to be atmospheric; presumably the mantle source region had equilibrated its gases with the atmosphere. The work reported here on three active ridge basalts shows the rare gases to be more primordial in nature; presumably the mantle source region has never seen the terrestrial atmosphere. The East Pacific seamount was shown by fission track dating to have erupted far from the active East Pacific ridge[7]. If further data show this difference in character between the rare gases trapped in open basin seamounts and those trapped in active ridge flows to be a general one, it is likely to be indicative of basically different magmatic histories in the two cases. As such, it will obviously have great bearing on models of mantle upwelling and seafloor spreading.

These data contain also the germ of detailed inferences concerning the state of degassing of the inner Earth, its mode of formation, and rare gas fractionation processes involved in planetary formation. Further studies should delineate both isotopic and elemental abundances and correlations (or lack of them) with ocean floor geography and plate tectonic models as well as with various mineralogical and eruptive parameters of the rocks involved.

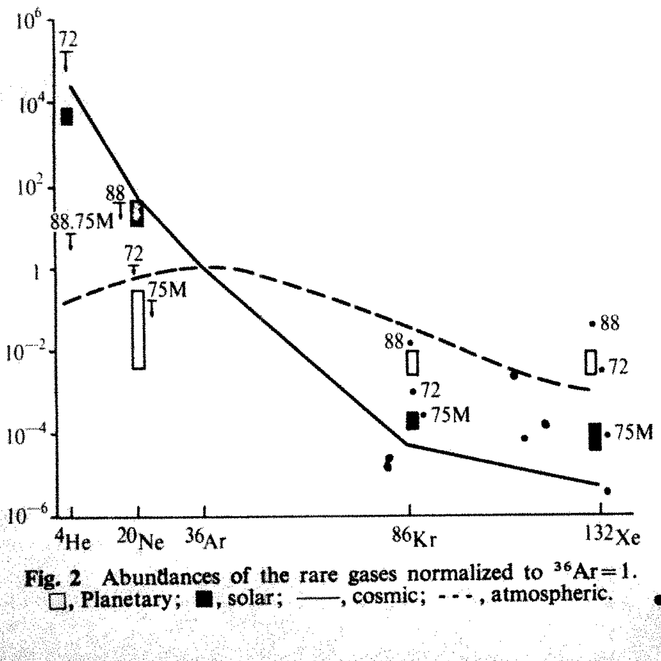

Fig. 2 Abundances of the rare gases normalized to ^{36}Ar = 1. □, Planetary; ■, solar; ——, cosmic; - - -, atmospheric.

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Contribution of Volcanic Sulphur Compounds to the Stratospheric Aerosol Layer

SULPHUR bearing compounds constitute a major portion of globally distributed persistent aerosol layer in the lower stratosphere[1-3] and some considerations[1] indicate that the particles are formed *in situ*, presumably by the oxidation of gases containing sulphur. The relative importance of various terrestrial sources, however, has not been ascertained.

Here we report a study of sulphur concentrations and the ^{32}S/^{34}S isotopic ratios of selected stratospheric and tropospheric aerosol samples in which we compared the relative values and observed trends with the dates and locations of major volcanic eruptions. More details, including an assessment of the importance of other contributing sources, will be given elsewhere[4].

Appropriate stratospheric aerosol samples, chosen with due regard to considerations of date, global location and height with respect to the tropopause, were obtained from existing libraries of the Health and Safety Laboratories of the USAEC and the Department of Defense. These samples were subjected to mass spectrometric analysis for isotopic enrichment; subsequently, concentration measurements were also made.

The results of our concentration measurements are shown in Fig. 1*a*. The times and approximate location of the important pyroclastic volcanic eruptions which have taken place during the past 10 yr in the equatorial latitudes are also indicated in Fig. 1*a*.

There is a clear correlation between sulphur concentration (expressed in μg of sulphate per standard m^3 of filtered air) and volcanic activity. Sulphate aerosol concentration in the Junge layer located south of the equator increased two orders of magnitude within a year after the catastrophic 1963 eruption of Mt Agung, at 8.5° S. Other data (not shown) reveal a similar effect for stratospheric aerosol samples collected during the same time period in the northern hemisphere from 1° N to 40° N. These data show that the sulphate contributions in the northern hemisphere from the eruptions of Agung, Taal, Fernandina, and Awu were all of about the same magnitude. Other samples collected in the Arctic (>55° N) stratosphere over the same time period and covering the eruptions of Trident (1963), Surtsey (1963), Sheveluch (1964), and Mt Redoubt (1966) exhibit the same dramatic increases in sulphate concentration.

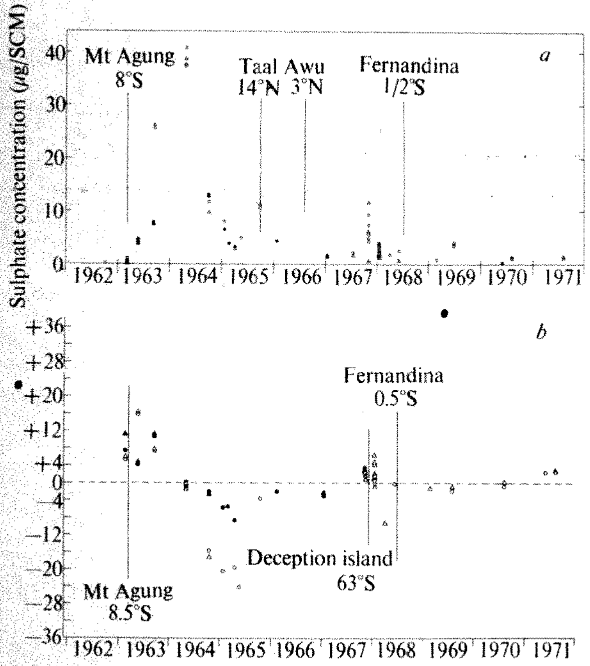

Fig. 1 *a*, Sulphate concentration as a function of time for stratospheric aerosols collected in the southern hemisphere (0° S to 43° S). *b*, Sulphur isotope ratios, del ^{34}S, 0° S to 43° S. All samples are corrected for trace sulphur background of the filter media. △, Corrected data where primary blank was available for direct determination; ○, cases where an average blank was used.

Isotopic ratios for the southern hemisphere aerosols are plotted in Fig. 1*b*. The cyclic trends in del values of samples collected subsequent to the eruptions of Agung and Fernandina are typical of those observed for samples taken in the north equatorial and Arctic stratosphere after the other eruptions mentioned. These data provide additional evidence for the source of the sulphate. To interpret the results, due consideration must be given to the isotopic composition of the tephra, as well as changes likely to result from gas-to-particle chemical reactions occurring during the residence of the gases after injection into the stratosphere.

The positive del values of the stratospheric samples collected shortly after the eruptions undoubtedly result from a weighted average of the value for the injected tephra, together with the limited quantity of particles formed by the conversion of gases to particles in the rising plume, and pre-existing material in the stratosphere. Several volcanic tephra samples were obtained from the Smithsonian Institute for recent eruptions of Hekla, Mt Mahon, Mt Arenal and Kilauea. Although not necessarily representative of all tephra, in each of these cases the del values were positive.

The subsequent abrupt decline in del value with time indicates a depletion of the ^{34}S isotope with respect to meteoritic sulphur for the aerosol particles being sampled. Such a change in ^{34}S enrichment of stratospheric sulphates suggests a fractionation of the isotopes of sulphur during exposure to a reactive chemical environment, and is thus indicative of chemical change. The direction that this change should take is difficult to assess theoretically, but a decrease in del value for the unreacted gas has been observed[5] experimentally and is also indicated by our results.

Within a month after an eruption, most of the coarse tephra has settled below the stratospheric sampling regions selected for this study. Therefore, we expect subsequent sampling to collect increasing amounts of particles produced from gases which were injected by the rising plume, as well as limited quantities of pre-existing particles settling from upper altitudes. Although the average residence time for particles in the stratosphere is about 1.5 yr, the average time of a particle spent at a particular altitude sample, even with due allowances for sampling height variations between missions, is comparatively short. Consequently, particles collected at progressively later times following an eruption represent those formed at higher altitude which have eventually settled into the sampling region.

As the injected gases diffuse upward, they are continually converted to particles from gas whose del value is progressively decreasing. Eventually, the gas converts to particulate matter; particles with progressively lower del values become concentrated at the higher altitudes. Because the upper layer particles require a longer settling time, the del value for samples collected in the lower stratosphere would be expected to show an increase followed by a decrease for some period of time after an eruption. After several years without a large eruption, the stratospheric isotopic ratio would be expected to return to an average value indicative of other contributing sources; such an effect is always observed, the average del value being 2.6±0.3 (our unpublished work with A. L. Lazrus).

This is confirmed by the data of Fig. 1. The solid points represent values of samples collected in the stratosphere at a lower (15.3 km) altitude between 40° S and 43° S, and the open points are samples collected at higher altitudes ranging from 18.3 to 19.8 km. Although the sulphate concentration values of these samples are in good agreement, the greater degree of ^{34}S enrichment for the lower altitude data is apparent.

So volcanic emissions represent the principal source perturbing the sulphate concentration of the stratosphere. Additional results[4] provide some evidence that upwelling Hadley cell circulation at the equator is an important source for that portion of the layer which persists in the absence of volcanic eruptions.

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Accurate Position of GX5–1 from Lunar Occultations

HERE we report the first observations of a lunar occultation of an X-ray source using detectors on board an Earth satellite. The source GX5–1 has now been located with an error box (95% confidence) of 6 × 20 arc s. A 2σ upper limit of 8 arc s has been put on the source diameter.

The source GX51 (2U1757–25) is the brightest of a class of powerful X-ray emitting objects lying in the galactic plane and concentrated in the direction of the galactic centre. Study of these objects, which are responsible for a large fraction of the total X-ray emission from our Galaxy, is impeded by the lack of any optical identification. The smallest error limits for the position of GX5–1 published so far[1] (~1.5 arc min) include a large number of stars and a weak radio source[2], which has been suggested as a possible counterpart.

The object GX5–1 is at present undergoing a series of lunar occultations[3]. Calculations of the track of the satellite Copernicus, which carries several X-ray telescopes constructed at MSSL, showed that on four occasions during the period March to August 1973, the satellite passes through the X-ray shadow of the Moon with respect to GX5–1 (using the position of GX5–1 as given by Schnopper *et al.*[1]). Both the disappearance (*D*1) and the reappearance (*R*1) of GX5–1 were observed on March 26, 1973; on April 22, 1973, although both disappearance (*D*2) and reappearance (*R*2) were visible to the spacecraft, the reappearance unfortunately occurred during the dead time of the spacecraft data-handling system. The observations thus yield three position lines on the celestial sphere whose common intersection is the most probable position of GX5–1.

The counts from each telescope (4 to 12 keV detector, 14 cm^2, 2 × 5 arc deg field of view, mechanical collimator; 1.4 to 4.2 keV detector, 3.7 cm^2, 12 arc min field of view, grazing incidence paraboloidal mirror; energy ranges are nominal, from preflight calibration) are accumulated in 62.9 s frames before being read out, successive frames being separated by a dead-time of 23.6 s. For the April 22 observations, the accumulated counts were read out every quarter frame, with no dead time between those subframe readouts.

Because GX5–1 is a strong source, the count rate from this source was far larger than the background count rate, both from the diffuse X radiation and charged particles, as measured while GX5–1 was occulted. A count intermediate between the background and full source rate was accumulated in those frames in which each *D* or *R* occurred. The high source to background ratio allowed an accurate determination of the fraction of a frame during which GX5–1 was in view. In this way timing accuracy much better than the frame duration was possible.

Background counts from charged particles were subtracted from all data before any further analysis (A. C. Fabian, private communication). The statistical uncertainty in the number of counts in each *D* or *R* frame dominated all other sources of error.

An upper limit to the size of a source can be derived from quarter-frame data because the occultation is observed in a single quarter-frame rather than spread out over several frames. The derived occultation time, for an extended source, would correspond to the position of the centroid of X-ray emission. The half width of the source would correspond to the time between the occultation and the beginning of the frame (or end, whichever is closer). This must be increased by the quadratic sum of the 2σ error in the occultation time and the maximum time into the adjacent frame that the start or end of an occultation of a diffuse source could have occurred and been masked by a 2σ statistical deviation.

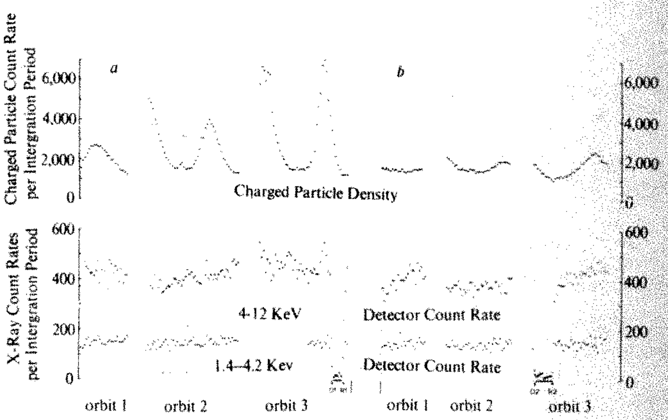

Fig. 1 Count rates of the 4 to 12 keV and 1.4 to 4.2 keV X-ray detectors before, during and after the lunar occultations on March 26, 1973 (*a*), and April 22, 1973 (*b*). Charged particle background has been subtracted. Also shown is the charged particle density as measured by the anticoincidence guard rate. Each point records the counts in a single integration period (62.9 sec). The points lie at 86.5 s intervals. The breaks in the data of each day represent GX5–1 going behind the Earth. The orbital period is 100 min.

The average source rate is constant in the 1.4 to 4.2 keV detector before and after each occultation (Fig. 1). All data obtained from this detector were used. The data from the 4 to 12 keV detector show marked secular variations. The derived event time turns out to be relatively insensitive to the choice of data used in determining the full source rate, but to reduce chances of systematic error only data observed directly before the occultations were used.

The Goddard Space Flight Center provided accurate orbital information which was combined with the time analysis described above to give the position of the satellite when each disappearance or reappearance was observed (listed, with error limits, in Table 1). These data, together with the lunar ephemeris in present use at the Royal Greenwich Observatory, were used to calculate the three positions of the lunar limb as viewed from the satellite at the appropriate times, *D*1, *R*1 and *D*2. A small correction of +0.4 arc s, taken from Watts's charts[4] of the marginal zone of the Moon, was applied to the position line to allow for the unevenness of the profile. In Fig. 2 the ±2σ error bounds of these positions are superimposed on an enlargement of the red Palomar Sky Survey print of the area. The contribution to these error bounds from the uncertainty in the satellite's longitude was minimized because on all three events the Moon was near the satellite's horizon, and

Table 1 Observation Times and Satellite Geodetic Coordinates with Standard Deviations (1σ)

Event	Date	UT (detector 1)	UT (detector 2)	UT (average)	Longitude (W)	Latitude (N)	Height (km)
*D*1	March 26, 1973	12 h 56 min 17.3 s ±3.2 s	12 h 56 min 18.0 s ±4.0 s	12 h 56 min 17.7 s ±2.4 s	48.54° ±0.03°	34.44° ±0.01°	745.5 ±0.5
*R*1	March 26, 1973	13 h 04 min 58.6 s ±4.0 s	13 h 05 min 02.2 s ±5.4 s	13 h 05 min 00.4 s ±3.1 s	15.83° ±0.03°	25.20° ±0.01°	741.4 ±0.5
*D*2	April 22, 1973	16 h 35 min 28.5 s ±0.7 s	16 h 35 min 30.4 s ±1.2 s	16 h 35 min 29.4 s ±0.8 s	285.70° ±0.03°	34.85° ±0.01°	737.5 ±0.5

therefore the satellite's motion in longitude was mainly directed towards the Moon. The 2σ error in latitude of ±0.02° contributed about ±1 arc s to the error bounds in Fig. 2. The area bounded by the intersection of the error bars is the best position obtainable from these occultation observations.

This position lies within the error circle given by Schnopper *et al.*[1] and on the edge of the 3U error box (R. Giacconi, private communication). None of the numbered stars in Fig. 1 of Kunkel *et al.*[5] lies within the new error box.

Table 2 Four Corners of Common Intersection Area in Fig. 3

RA (1950.0)	Dec (1950.0)
17 h 58 min 03.1 s	−25° 04′ 39″
03.4 s	41″
04.4 s	29″
04.9 s	16″

The occultation data set a 2σ upper limit of 8 arc s on the angular diameter of GX5–1, substantially below the limit given by Schnopper *et al.*[1]. The 3U catalogue (R. Giacconi, private communication) reports variability by a factor of 2, indicating that GX5–1 is likely to be a compact source. Our observations showed variations of up to 38% from day to day and up to 10% in a given day (Fig. 1). Rappaport *et al.*[6] have analysed data on GX5–1 for fast time variations and have set an upper limit of 3% on the pulsed fraction over the period range 10 ms to 15 s.

Figure 3 is a diagram of the region of intersection of the 2σ occultation bounds together with the positions of nearby stars and a faint radio source. The positions of stars 21 and 22 and the radio source are taken from Braes *et al.*[2]. The positions of stars 7, 23 and 24 were determined at the RGO on a photographic negative of the Palomar chart printed onto a glass plate and measured in the usual way, using several bright field stars to derive the scale and orientation of the plate. The positions so derived have a 2σ error on ±2 arc s. There are no objects near the 2σ occultation limits on the Palomar red plate other than those shown in Fig. 3. Star 23 is not visible on the blue plate, 24 is just visible, and 7, 21 and 22 are clearly visible.

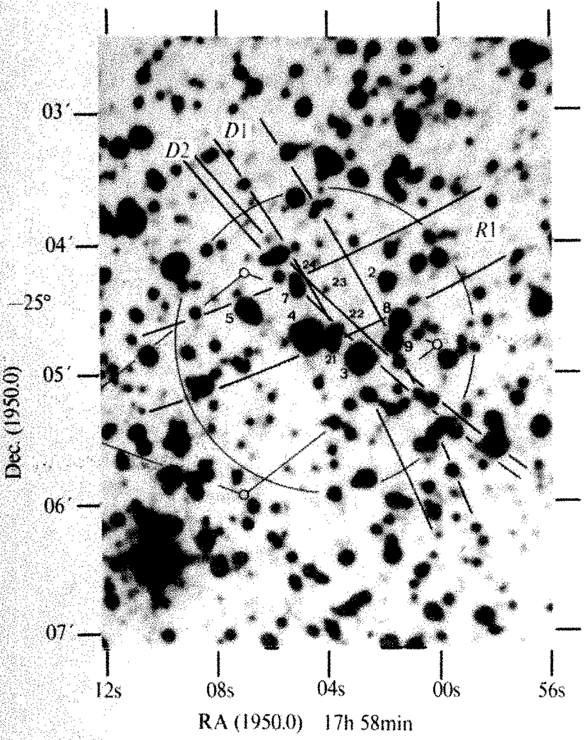

Fig. 2 Enlargement of Palomar Survey red print (copyright National Geographic Society) showing the intersection of the ±2σ limits for the three occultation events *D*1, *R*1 and *D*2. The error circle of radius 1.2 arc min due to Schnopper *et al.*[1] and the 3U 90% limits (private communication), represented by small open circles, are also shown. Star numbers up to and including 9 are those assigned by Kunkel *et al.*[5]; we have assigned numbers 21 to 24. Star 23 is close to the limiting photographic magnitude of 20 mag on the original print.

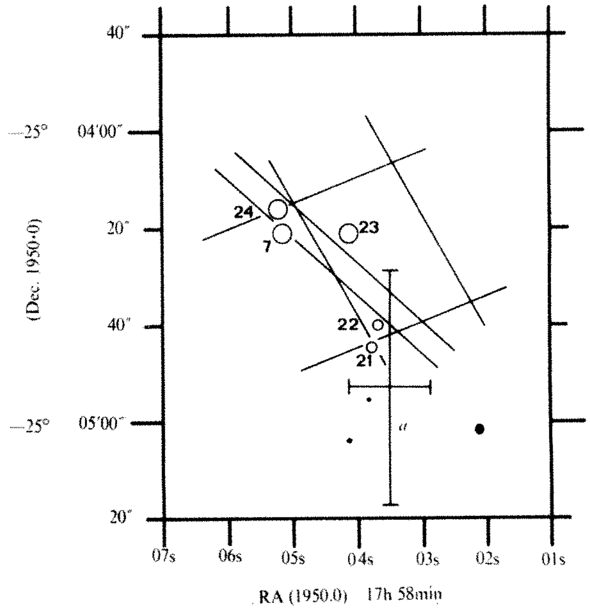

Fig. 3 Diagram of the intersection region in Fig. 2. ○, Measured star positions down to the limiting magnitude of the Palomar print. The positions for 21 and 22 are due to Braes *et al.*[2] and those for 7, 23 and 24 were measured at the RGO as described in the text. The position of the faint radio source given by Braes *et al.*[2] is also shown (*a*). All error bounds in the figure are at the ±2σ level.

Although the lack of a conspicuous object in the error box is disappointing, it is not unexpected if GX5–1 really is near the galactic centre. A distance of 12 kpc is implied if the low energy cutoff of GX5–1 is caused by absorption through an interstellar column density $N_H = (2.5 \pm 0.5) \times 10^{22}$ H cm^{-2} (refs. 6 and 7). Tarenghi and Reina (ref. 8 and private communication) show that the interstellar dust associated with this amount of gas would produce a visual extinction $A_v = 15 \pm 3$ mag. But if GX5–1 were associated with a binary system whose primary was a BO star with $M_v = -6$ there would be a possibility of seeing it. The secondary in the system would be too faint to be detected, but the primary, while not present on a Palomar Survey blue plate, would be at the limiting magnitude of the corresponding red plate. This model would make the proximity of stars 7, 21, 22 and 24 to the error box probably fortuitous.

We note the similarity between GX5–1 and GX3+1. Both are bright, variable X-ray sources with low energy cutoffs indicating distances on the order of 10 kpc. The revised lunar occultation position[9] of GX3+1 shows no bright stars in the error box but lies near a weak radio source, just like GX5–1.

The maximum visibility of the double star system described above would be at a wavelength ⩾2 μm. Thus the best future prospects for optical identification of GX5–1, GX3+1, and presumably the other similar galactic centre X-ray sources, would be an extension of the optical search to infrared wavelengths and simultaneous X-ray, infrared and radio observations to look for correlated time variations.

J. A. H. is a NATO postdoctoral fellow. P. J. N. D. is an SRC postdoctoral fellow.

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Correction to the Position of GX3+1

WE have previously given the results of two lunar occultations[1] of the X-ray source GX3+1. Only two optical objects were nearby, both outside the error box. The only one of these which looked to be a serious optical candidate has been shown[2] to possess no unusual properties which could indicate that it had a strong X-ray emission.

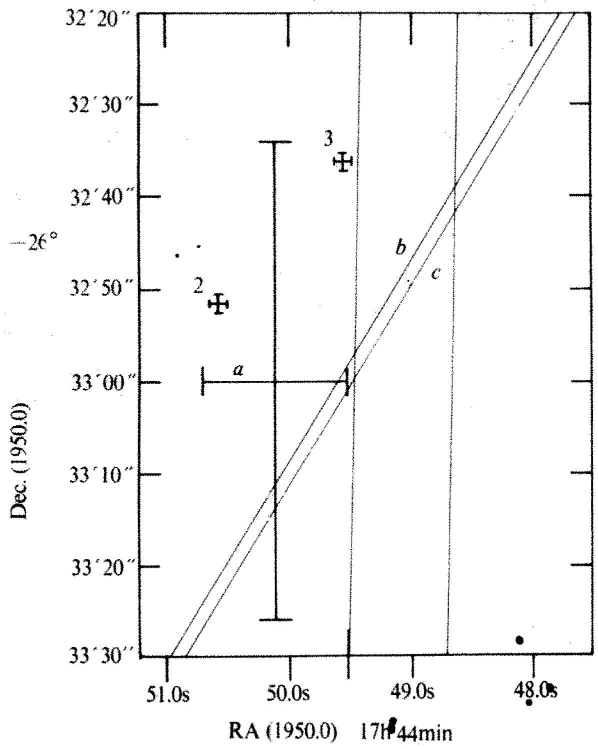

Fig. 1 The lines represent the 2σ error limits of the positions of the source obtained from each experiment; the radio and optical sources also have error limits of 2σ shown to their positions. *a*, Radio source; 2 and 3, Kunkel's objects[3]; *b*, Leicester observations; *c*, MSSL observations.

Recently the original X-ray data have been checked and the discovery of a timing error has resulted in a shift of about 2.5 s (RA) in the MSSL position. This is equivalent to moving the intersection position about 1 arc min along the Leicester error box; the new position is shown in Fig. 1.

There is no optical object in the new overlap position; Kunkel's objects "2" and "3" (ref. 3) lie too far away to be considered. A search for a radio counterpart at the Leiden Observatory (G. K. Miley, private communication) has shown that a weak source (11±4 m.f.u. at 1,415 MHz) exists at RA 17 h 44 min 50.15±0.2 s, Dec—26° 33.0′±0.25′ (1950). This source, with its 2σ error bars, is shown in Fig. 1. It is very close to the centre of the error box quoted by Schnopper *et al.*[4] and is of similar strength to possible radio candidates for GX5−1 (10±3 m.f.u.)[5] and Cyg X−1 (24±4 m.f.u.)[6].

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BIOLOGICAL SCIENCES

Effects of Contraceptive Pill Constituents on Foetal Mouse Hearts

ALTHOUGH the use of the contraceptive pill carries a slight risk, it is generally felt that the harmful side effects are outweighed by the benefit of avoiding unwanted pregnancies. Following the thalidomide tragedy, there is a wider appreciation of the risk of substances taken during pregnancy injuring the foetus. As we now have a direct method of studying the action of drugs on the foetal heart[1], we felt that it was advisable to see whether a pregnant woman who started taking the pill would jeopardize her foetus.

In this initial study we took foetal hearts from pregnant mice and cultured them by the well established technique instituted by H. Fell and consolidated by K. Wildenthal[2]. Eight groups of twenty mouse hearts were used to test hormones commonly used in the pill at the probable achieved concentrations. Forty control hearts were used and a further twenty hearts were used to check that the ethanol solvent for the hormones did not affect the results.

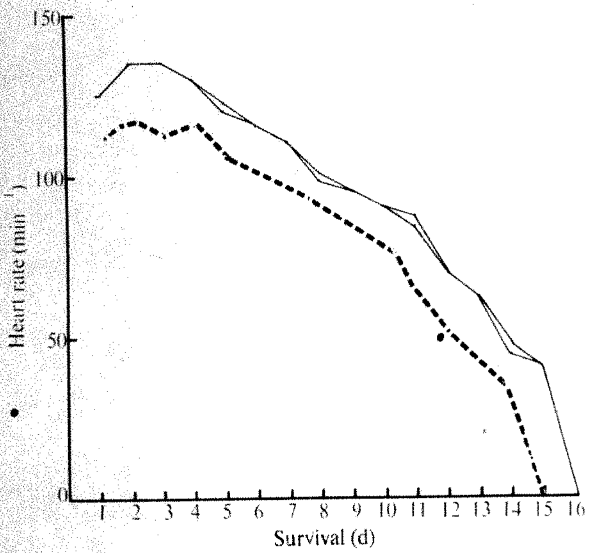

Fig. 1 The enhancing effect and increased survival of hearts cultured with 1 µg of ethinyloestradiol.

Following a previous technique[3], 9 and 15 d foetuses were removed aseptically from freshly killed pregnant mice. The heart and lungs were removed and transferred to sterile Petri dishes under a dissecting microscope. The heart was dissected from the lungs, the pericardium and blood vessels were carefully trimmed away and residual blood was washed from the organ with culture medium. The isolated hearts were then placed on a stainless steel grid, the larger ones directly and the smaller ones on sterile filter paper (Whatman No. 1), so that the lower side of the organ was exposed to 2 ml of culture medium in the 30 mm × 13 mm Petri dishes and the top to the atmosphere. The small Petri dishes were placed in 90 mm × 13 mm Petri dishes, a filter paper soaked with water placed on the bottom to increase humidity and they were covered with a loose fitting lid. The cultures were placed on racks in airtight McIntosh jars filled with an atmosphere of 95% oxygen and 5% carbon dioxide[4]. They were kept in incubators at 37° C±0.5° C. The medium and atmosphere were renewed every 24 h.

The hormones tested were ethinyloestradiol (1 µg and 10 µg), norgestrel (1 µg and 10 µg), norethisterone acetate (1 µg and 10 µg), a combination of 1 µg ethinyloestradiol and 1 µg norethisterone acetate and a combination of 10 µg ethinyloestradiol and 10 µg norethisterone acetate.

The eight hormones, in 0.2 ml of 1% ethanol, were added to a medium which consisted of 199 medium (65%), foetal calf serum (35%, Wellcome Reagents Ltd), cortisol (0.1 µg ml^{-1}), insulin (50 µg ml^{-1}), penicillin (100 units ml^{-1}) and streptomycin (0.1 mg ml^{-1}) to total 100 ml.

Ethanol (0.02 ml%) caused no demonstrable change in the beating or survival period of the hearts, when compared with the controls. Ethinyloestradiol (1 µg) in 100 ml produced an increase in heart rate and a 1 d increase in survival time when added to the culture medium. Ethinyloestradiol (10 µg) had less effect on the rate than 1 µg with no increase in survival. Norgestrel (1 µg) added to the culture medium caused an increase in rate, an obvious increase in the force of contraction of both atria and ventricles, and a 3 d prolongation of the survival period.

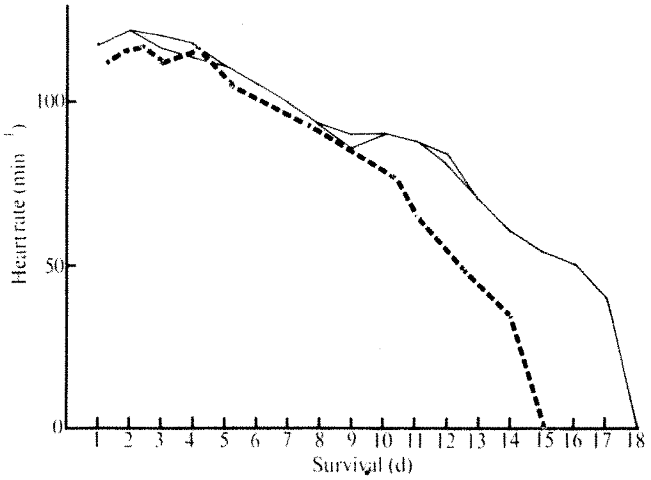

Fig. 2 Increased survival time with little early increase in beating, with 1 µg norgestrel.

Norgestrel (10 µg) also affected the hearts, increasing their rates, force of contraction and survival period, but to a lesser extent than 1 µg and prolonging survival by only 1 d. Norethisterone acetate (1 µg) caused an overall slowing of the heart rates and force of contraction and a 1 d reduction in survival time. Norethisterone acetate (10 µg) produced a definite decrease in rate and force of contraction of atria and ventricles at all stages, as well as a 3 d shortening of survival period. At this concentration, norethisterone acetate had a greater depressant effect than the 1 µg concentration. Ethinyloestradiol (1 µg) and 1 µg norethisterone acetate appeared to antagonize each other, resulting in a performance similar to the controls. Ethinyloestradiol (10 µg) and 10 µg norethisterone acetate decreased the rate compared with controls.

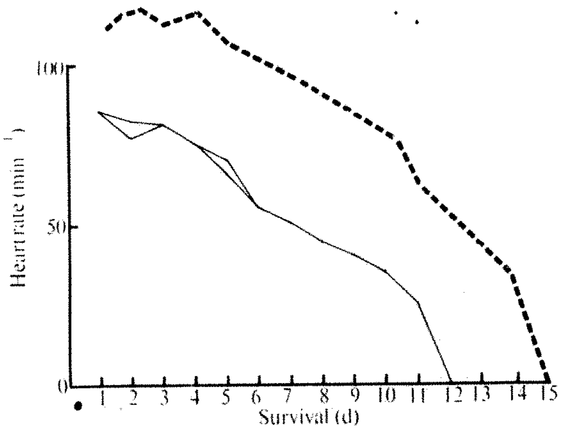

Fig. 3 Profound depressant effect and reduction in survival time with 10 µg norethisterone acetate.

Of the individual hormones studied, 1 µg norgestrel had the greatest enhancing effect on survival and performance whilst 10 µg norethisterone acetate had the greatest depressant effect on both parameters. The lesser enhancing effects of ethinyloestradiol appear to virtually cancel the depressant effects of norethisterone acetate in the concentrations studied. This combination was chosen for study because, in various proportions, it is the commonest used in the formulation of contraceptive pills. Norgestrel is less commonly used as "Progestogen", in combination with oestrogens, in the pill and so was not studied in combination with them.

Table 1 Performance of Foetal Hearts Exposed to Test Hormones Compared with Controls

Substance	Survival	Rate	Force of contraction
Solvent	No detectable change		
1 μg Ethinyloestradiol	+1 d	↑	—
10 μg Ethinyloestradiol	—	↑	—
1 μg Norgestrel	+3 d	↑ ↑	↑ ↑
10 μg Norgestrel	+2 d	↑ ↑	↑ ↑
1 μg Norethisterone acetate	—	↓	↓
10 μg Norethisterone acetate	−2 d	↓ ↓	↓ ↓
1 μg Ethinyloestradiol + 1 μg norethisterone acetate	—	—	—
10 μg Ethinyloestradiol + 10 μg norethisterone acetate	—	↓	—

Number and direction of arrows indicate magnitude and type of response.

If inferences can be drawn from this preliminary study using mouse foetal hearts, it would seem that the concentration of norethisterone acetate in the pill should be kept to a minimum. When the current problems of obtaining human foetal material are overcome, this study will be repeated using human foetal hearts.

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Enhancement of Metabolic Coronary Dilatation by Aspirin-like Substances by Suppression of Prostaglandin Feed-back Control?

IN the isolated, perfused heart, increased activity induced by catecholamines and/or calcium ions is followed by enhanced coronary flow, attributable to some metabolic process in the myocardium. This metabolically induced coronary basodilatation (MCD) is inhibited by prostaglandin E_1 (ref. 1). The increased MCD response correlates with 3′5′-cyclic AMP levels. Furthermore, when prostaglandins (PGs) are infused, inhibition of MCD correlates with diminished cyclic AMP production[2,3]. The inhibition of MCD by exogenous administration of PGs suggests that these autacoids may play a role as modulators of the coronary reaction to increased cardiac activity[4]. If it were possible to demonstrate the participation of PGs produced endogenously, their relevance in this modulatory mechanism of adaptation of coronary flow would become evident.

As indomethacin and aspirin have been shown to inhibit PG synthesis[5–7], we investigated the actions of these substances on the MCD which follows the increase of cardiac activity produced by noradrenaline, Ca^{2+} (ref. 8) and tachycardia.

Male Wistar rats, weighing 240–265 g, were anaesthetized with ether and the hearts were isolated and perfused by the Langendorff method at 50 mm Hg perfusion pressure. The Krebs-Henseleit bicarbonate perfusate contained one half the usual calcium concentration[9] and was gassed with $O_2 : CO_2$ (95 : 5). Phentolamine (400 $\mu g\ l^{-1}$) was added to the perfusate to inhibit an adrenoceptive action of noradrenaline. The force of contraction was measured by attaching a clip to the ventricular apex and connecting it to a force displacement transducer (Grass FT.03) under 2 g initial tension and coronary flow was measured continuously by a modified flowmeter[10] and recorded on a polygraph. The interventricular septum was clamped and, with a dipolar electrode placed on the surface of the right ventricle, the heart was stimulated at 210 beats min^{-1} with square wave pulses (5 ms duration, current approximately 20% above threshold). By pacing the heart it was possible to achieve uniform cardiac activity and also to avoid changes of heart rate due to noradrenaline. The effect of tachycardia was studied by pacing the heart at 250 beats min^{-1} for 30 s.

Increments in coronary flow produced by noradrenaline, Ca^{2+}, adenosine or tachycardia were assessed by planimetry of the area under the flowmeter tracing from the beginning of dilatation until the point at which the coronary flow had returned half way from maximum response to control level (Fig. 1). At the end of each experiment, of approximately 60 min duration, the heart was removed, blotted and weighed (mean wet weight 1.01 ± 0.024 g). Single doses of noradrenaline (7 ng and 9 ng), $CaCl_2$ (10 μg and 20 μg) and adenosine (0.2 g) in volumes of 0.1 ml were administered by aortic cannula. Aspirin and indomethacin were infused at the rate of 0.1 to 0.2 ml min^{-1} while the PGE_2 was added to the perfusate reservoir. Significance of changes was calculated by the *t*-test for paired data.

The basic coronary flow for the series, shown in Fig. 2, was 6.8 ± 0.25 mg g^{-1} min^{-1}. Administration of noradrenaline caused dose dependent inotropic effects and proportional increases in MCD. In most of the experiments, coronary dilatation developed without a preceding decrease in flow (Fig. 1*a*). In spite of the presence of phentolamine, a phase of reduced flow preceded the dilatation in some experiments (Fig. 1*b*). This reduced flow is attributed to the increased "extravascular support" leading to the increased impedance to flow[10]. Similar observations were made on the administration of Ca^{2+} or during tachycardia (Fig. 1*c*, *d*). The initial reduction of coronary flow in response to Ca^{2+} could also be attributed to both vascular smooth muscle contraction[11–13] and to increased "extravascular support"[14].

Aspirin was infused at a rate of 90–108 μg min^{-1} and indomethacin at 10–40 μg min^{-1}. Assuming the mean control coronary flow rate, the final drug concentrations in the perfusate were 0.076 to 0.15 mM and 0.0042 to 0.017 mM, respectively. These concentrations are of the same order as those found to be effective in inhibiting synthesis of PG[5,15–17]. The basic coronary flow during infusions of aspirin was 6.6 ± 0.25 ml min^{-1}, and with indomethacin at 10–20 μg min^{-1}, it was 6.6 ± 0.52 ml min^{-1}. At the highest dosage of indomethacin, 40 μg min^{-1}, there was at first a gradual increase in coronary flow that later subsided to 6.5±0.17 ml min^{-1}. After only 5–10 min infusion of either drug, a clear potentiation of MCD responses to challenging doses of noradrenaline, Ca^{2+} or to tachycardia was observed at all concentrations studied. The effects of full potentiation obtained after approximately 20 min of infusion are shown in Fig. 1 and the data for the series are tabulated in Fig. 2.

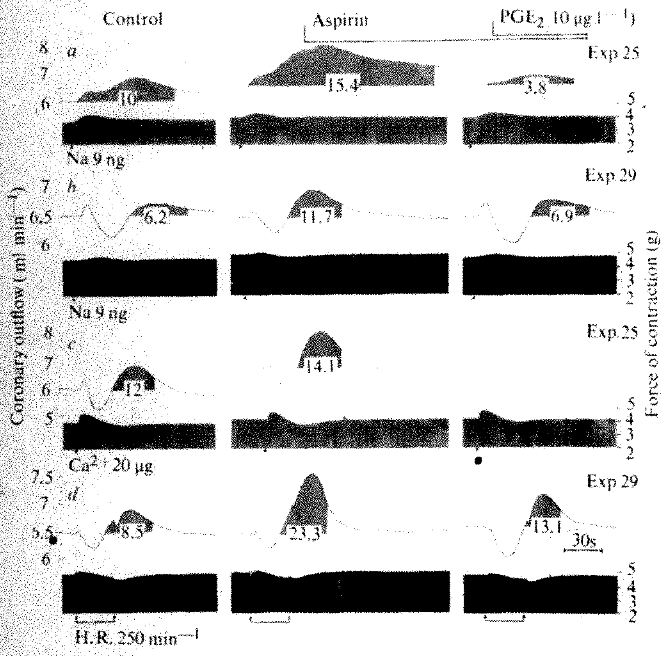

Fig. 1 Effects of aspirin before and during PGE_2 infusion on MCD responses. The calibrations on the left refer to coronary outflow, the hatched portion represents the area measured for MCD responses and the numbers within the hatching denote % change from control level. The right hand calibration represents the force of heart contractions. Doses of noradrenaline (Na) and calcium chloride (Ca^{2+}) were given (▲). Tachycardia (250 beats min^{-1}) was applied during the interval (↑____↑).

Aspirin and indomethacin affected only the MCD response, as cardiac hyperactivity produced by noradrenaline, Ca^{2+} or tachycardia was not affected. In a few experiments where the aspirin infusion was stopped, the enhanced MCD response continued for over 45 min.

The enhancement of MCD by aspirin or indomethacin was so predominant that a less pronounced phase of initial decrease of flow was observed (Fig. 1*b*, *c*, *d*). In the absence of this initial decreased flow the normal MCD response is enhanced to a greater extent (Fig. 1*a*).

When stable potentiation of MCD was reached, perfusion with PGE_2 at a concentration of 10 µg l^{-1} was initiated without interrupting the infusion of aspirin or indomethacin. On addition of PGE_2 the coronary flow increased but subsided to within control limits (6.43±0.36 ml g^{-1} min^{-1}) after about 10 min. After 15–20 min of PGE_2 infusion, there was a marked inhibition of the MCD responses (Figs. 1, 2). Again the cardiac hyperactivity induced by tachycardia or by challenging doses of noradrenaline or Ca^{2+} was unaffected by addition of PGE_2. Furthermore, it seems that this inhibitory action is specific for the MCD response, as the vasodilatory effects of adenosine were not affected by aspirin. Increase in coronary flow with adenosine was 7.3±2.71% and with adenosine plus aspirin 6.8±1.17% ($P>0.1$).

It seems that coronary vasodilatation, leading to improved coronary flow, is one of the major adaptative mechanisms of intracardiac origin that permit the coronary circulation to compensate for increased metabolic demands because of increased cardiac activity. As increased levels of cyclic AMP correlate with the MCD response to cardiac hyperactivity[3], it is our belief that cardiac hyperactivity leads to activation of adenyl cyclase and that this is the triggering mechanism which controls the tone of the coronary vascular smooth muscle of the coronaries. This belief is supported by the observation that if cyclic AMP levels are lowered by inhibiting adenyl cyclase activation with PGE_2, cardiac hyperactivity is then followed by a reduced MCD response[2]. If phosphodiesterase inhibitors are administered to the rat heart, however, potentiation of MCD and increased levels of cyclic AMP occur[2,3].

It has been shown that synthesis of PG may be elicited by noradrenaline administration or by sympathetic nerve stimulation[15,18] and that this synthesis can also be inhibited by aspirin or indomethacin[19]. PG inhibits the release of catecholamines, and it has been postulated that PG plays a role as a feedback braking system which controls the release of noradrenaline from adrenergic nerve endings[20,21].

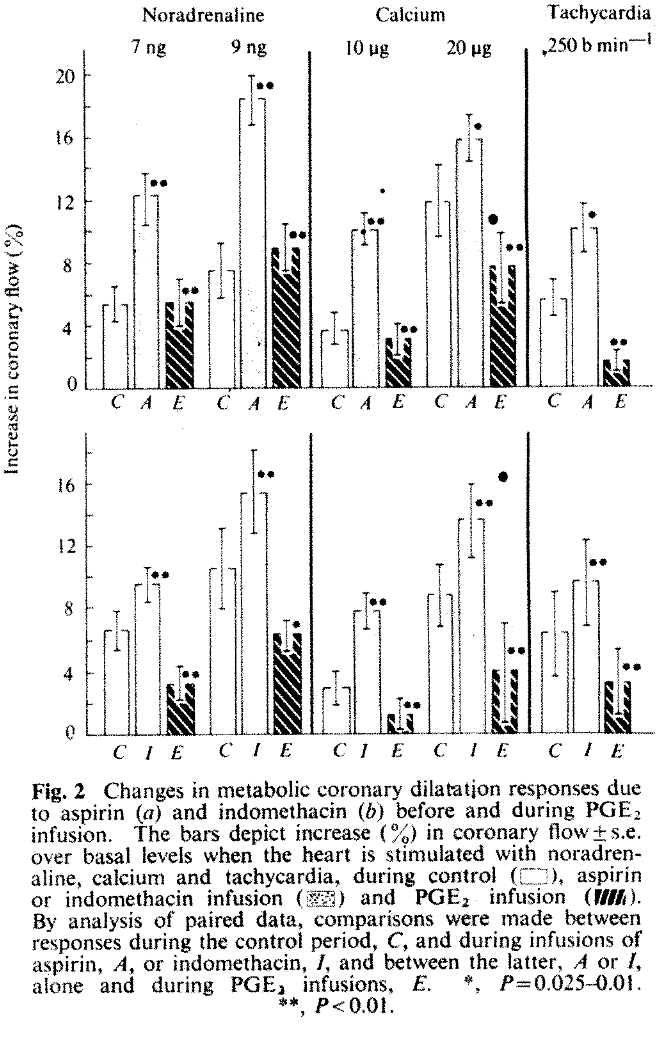

Fig. 2 Changes in metabolic coronary dilatation responses due to aspirin (*a*) and indomethacin (*b*) before and during PGE_2 infusion. The bars depict increase (%) in coronary flow±s.e. over basal levels when the heart is stimulated with noradrenaline, calcium and tachycardia, during control (☐), aspirin or indomethacin infusion (▨) and PGE_2 infusion (▨). By analysis of paired data, comparisons were made between responses during the control period, *C*, and during infusions of aspirin, *A*, or indomethacin, *I*, and between the latter, *A* or *I*, alone and during PGE_2 infusions, *E*. *, $P=0.025$–0.01. **, $P<0.01$.

We have hypothesized that endogenous PGs are physiological modulators of the metabolic coronary dilatation which occurs in response to cardiac hyperactivity, whether induced by noradrenaline or other means. That is, PG mediates a braking system on the adenyl cyclase activation[22]. Suppression of PG synthesis therefore results in increased cyclic AMP production and so in the augmented metabolic coronary dilatation. The latter cannot be attributed to the release of PG as it is the inhibition of that release which leads to enhanced MCD. Inhibition of PG synthesis does not change the dilatation produced by exogenously administered adenosine and so the latter is not likely to be a mediator of the metabolic coronary reaction.

From our concept, we would expect that failure of metabolic coronary dilatation should lead to coronary insufficiency whenever the heart is strained. If this is correct, one may postulate that the administration of an aspirin-like compound or other inhibitor of PG synthesis[20] would be useful in preventing coronary insufficiency in conditions of cardiac stress.

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Chemical and Mechanical Requirements for Fibroblast Adhesion

HERE I show that fibroblasts do not adhere to a rigid hydrophobic or yielding hydrophilic surface. There are three aspects; clean surfaces, the smallness of the adhesion sites, and mechanical stresses exerted by the cell.

Surfaces are listed in Table 1 according to wettability[1]. Cells spread fully on glass and oxidized polystyrene, less readily[2] on polyester, and only patchily on, for example, native polystyrene and polyethylene. It was concluded[1] from a discrepancy in surface energies between polyethylene and pure paraffin that "even the best specimens of polyethylene have traces of polar, strongly water-attracting material present in or near their surfaces". These polar heterogeneities, if small and dispersed, may remain undetected by the drop method for measuring surface energy[1,3] because the drop, mm in diameter, is a less localized probe than the cell which makes adhesive "plaques" of only 1 μm[4].

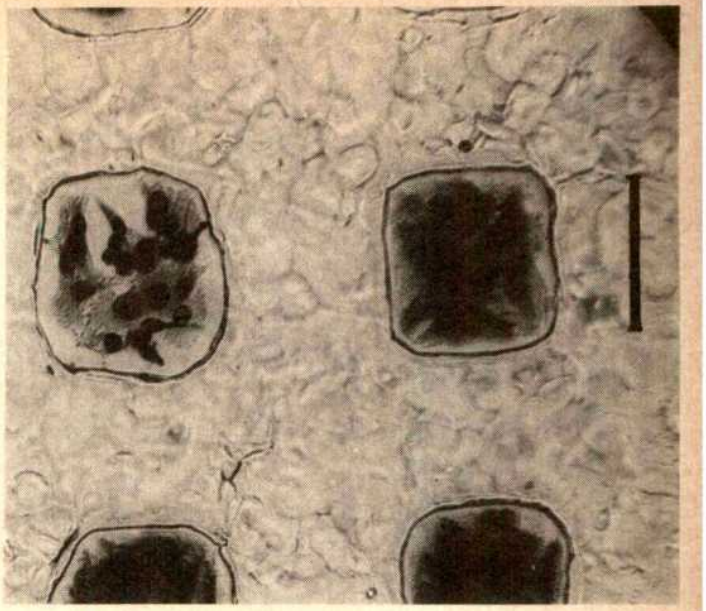

Fig. 1 "Haptotactic islands" of tissue culture surface, with spread cells surrounded by a non-adhesive surface of solid paraffin. Bar = 100 μm.

Hypothetically, cells should not be able to spread on a surface of solid paraffin, free from polar impurities. Paraffin waxes were dissolved at 5% v/v in hexane, and polar material was extracted by shaking with Al_2O_3 (BDH Ltd) before use; 0.1 ml was dried on a 3 cm polystyrene tissue-culture dish. Cells were added (10^5 BHK or 3T3, in 2 ml medium with 10% calf serum) and incubated for 3 days at 37° C. Paraffin was found to be non-adhesive for mouse and hamster fibroblasts.

Table 1 Surface Energies of Some Materials in Tissue Culture[1]

Material	Surface energy (dyne cm^{-1})
Fluoropolymer	19
Paraffin ($-CH_3$)	23
Polyethylene	31
Polystyrene (native)	33
Polyester	43
Polystyrene (corona-treated)	56
Water	72
Glass	About 700

Samples with melting point 55–65° C were satisfactory, but those with a melting point of 49° C softened in the incubator, and retracted from the hydrophilic tissue culture surface. This suggested a convenient method of preparing "haptotactic islands"[5] for dividing the growth surface into shaped colonies. An electron microscope grid (Smethurst Ltd, Bolton) was dipped into paraffin solution, and laid in a tissue culture dish at 50–60° C. The paraffin melted and retracted from the holes of the grid, but remained in position under the surrounding metal surface. After cooling the grid was peeled away, leaving its paraffin replica outlining hydrophilic "islands" on the dish (Fig. 1). The film can be scratched to expose the underlying tissue culture surface; cells will attach a migrate in such a track.

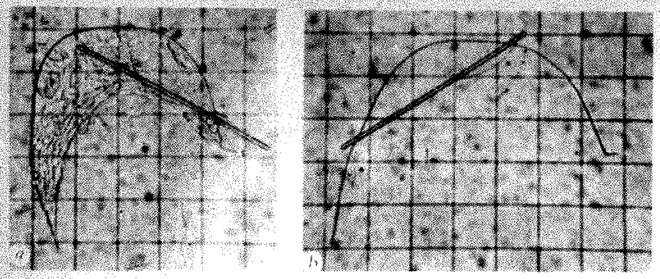

Fig. 2 Demonstration that fibroblasts exert tension on their substrate. BHK C13 cells were mixed with fine glass fibres (Whatman GF100) and grown in drops of medium, under paraffin oil, on a bacteriological polystyrene dish. Cells were lysed by adding a drop of detergent (SDS in 0.2 N NaOH). *a*, Curved fibre, spanned by a web of cells; *b*, same fibre, after lysis of cells. Scale: 1 division = 100 µm.

Agar is hydrophilic. Why do cells not normally spread on it[6,7] while they will extend both on and in a gel of dilute collagen[6,8]? Agarose molecules form an interlacing network of hydrogen-bonded double helices, with periodic "kinks" in each molecule, which prevent complete pairing between any two strands of the helix, ensuring that they will branch off and form new helices with at least one other partner[9]. This intercoiled molecular structure leads to a gel which is macroscopically solid, resilient, and precise in shape, but which, on the cellular scale, may be a diffuse "ethereal haze"[10], unable to support a concentrated load. Collagen molecules associate in long, 3×5 stranded helices, side by side in dense, straight filaments[11], 0.01–0.1 µm thick. Macroscopically, collagen gels are liable to collapse[8] but, on the cellular scale, the fibres offer localized support. (Thus a gel of collagen fibres in agar would be a crude model of connective tissue: in cartilage, collagen provides strength and rigidity, while mucopolysaccharides govern resilience and permeability[12].) The electron microscopy of agar, collagen and the cell coat, and their mechanical interactions, have been discussed[13,14].

We have found[15] that isolated fibroblasts in agar, if they are allowed to stretch in one dimension, will grow on fine glass fibres (Whatman GF100), 0.05–0.5 µm thick. The thinner fibres of glass approach collagen dimensions; that fibroblasts will stretch on them is further indication of the localized extent of cell adhesion to substrates. The bowed shape of some fibres suggests that the cells exert tension because the bows straighten if the "strings" are lysed (Fig. 2).

I postulate that fibroblasts require a rigid scaffolding to withstand tension generated by their stretching. Glass, or the fibres in a collagen gel, even if much thinner than the cell, can provide such a scaffolding; more diffuse gels cannot. (Cells will spread, although imperfectly, on dried agar[16].)

The observation that cells do not spread on a film of calf-brain phospholipid[17] can be explained. Membrane lipids are fluid and orientate with hydrophilic groups towards water. Mechanically, multilayers of calcium stearate resist normal load, but break up under transverse load, so that sliding occurs within a mush of stearate[13]. Phospholipid films therefore may provide another example of a hydrophilic surface of low yield strength.

Experimentally, egg lecithin (BDH) was found to form a non-adhesive substrate, applied as 0.1–0.2 ml of a 1% solution in hexane. Unlike paraffin, this phospholipid surface was readily wetted. When scratched in medium containing serum at 37° C, the lecithin layer displayed, under the microscope, the consistency of a thixotropic, viscoelastic fluid. Cells did not attach to the layer, but readily grew in tracks scratched through it.

It might be supposed that, if cells do not adhere to a hydrophobic surface, and do not spread on a yielding surface, then the least adherent interface would be that of a hydrophobic fluid. Cells grow, however, on the interface between medium and droplets of silicone oil. The solution to this paradox is found by probing the interface with a finely drawn glass fibre under the microscope. The surface of the oil drop puckers, and the fibre bends. A skin can be seen which consists of denatured serum proteins, which, with hydrophobic interiors now exposed to the oil, bridge the great gap in surface tension (40–50 dyne cm^{-1}) between oil and water. Such skins accumulate readily, even at the interface between purified liquids, withstand considerable shear forces[18], and provide a rigid hydrophilic surface on which cells can spread. Conversely, the amphipathic, neutral, lecithin surface shows little tendency to adsorb and denature proteins[19], producing the mobility of the phospholipid interface, compared to that of an oil, in serum.

That the cell's attachment sites seem to be hydrophilic and small agrees with the detection of dense ruthenium-red staining (that is, acid polysaccharide) material at plaques, both *in vitro* (S. Pegrum, personal communication) and *in vivo*[10]. As for exerting tension, microfilaments, possibly contractile, have been observed in the cytoplasm, pointing towards attachment plaques near the leading edge of the cell[4].

The alkane surface, with its CH_3- and CH_2-groups, is a chemically defined base line; by systematic introduction of other components, it should be possible to obtain a more detailed picture of the chemical bonds involved in cell adhesion. Because the surface is rigid, one can vary not only molecular concentration, but also spatial distribution. Clustering may be important for cells to make strong, localized bonds.

It is notable that, of the two non-adhesive, hydrophilic substrates, agarose is uncharged and phosphatidyl choline is an almost neutral zwitterion[20]. Adhesiveness, even in the absence of like charges, can be decreased by the exclusion volume[21] whereby one randomly coiling molecule tends to oust another: this effect might explain reduced adhesion in serum[18].

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Evidence that Cyclic AMP Does Not Mediate the Action of Gibberellic Acid

Many animal hormones operate by increasing the intracellular level of cyclic AMP, which then acts as a second messenger to elicit a variety of physiological effects within the cell[1]. There is no conclusive evidence that cyclic AMP performs a similar function in higher plants. Exogenously supplied cyclic AMP can mimic certain effects of plant hormones[2–4], but the responses do not equal the full effect of the hormone itself and may be pharmacological. Reports that plant hormones can elevate cyclic AMP levels in plant tissues[5,6] lack sufficiently rigorous proof that the factor being measured is indeed the cyclic nucleotide. The criteria of identity most frequently employed, selective precipitation[7] and cochromatography, are inadequate to resolve pmol quantities of cyclic AMP from nmol or µmol of other adenine nucleotides. I have investigated the possibility that cyclic AMP is synthesized in response to gibberellic acid (GA) in barley aleurone layers. I have measured the incorporation of ^{14}C-adenosine into cyclic AMP in barley aleurone layers, and my results do not support the suggestion that the cyclic nucleotide mediates the action of GA[2,3,5].

GA induces the synthesis of α-amylase in isolated barley aleurone layers, the enzyme first appearing after a lag phase of 6 to 8 h (ref. 8). GA at 10^{-6} M accelerates the synthesis of α-amylase some thirty-fold. An increase in the level of cyclic AMP should precede the GA response if cyclic AMP mediates that response[9]. To demonstrate any effect on cyclic AMP synthesis during GA treatment, the hormone must be applied at a time when endogenous ATP is adequately labelled by applied ^{14}C-adenosine. In barley aleurone layers, labelled adenosine (94 nmol per 100 layers) equilibrates into endogenous ATP within 12 h of incubation (Fig. 1). In the experiments below, I used a uniform incubation period of 12 h with U-^{14}C-adenosine (50 µCi, 94 nmol per 100 layers) at high specific activity (534 mCi mmol^{-1}, Amersham-Searle). GA was added for various periods from 0 to 8 h before termination of incubation.

Cyclic AMP was isolated by grinding aleurone layers at 0° C in 10% trichloroacetic acid (TCA) containing 8-^{3}H-cyclic AMP as internal standard (approximately 240,000 c.p.m. per 100 aleurone layers). Debris and precipitated protein were removed by centrifugation and protein in the pellet was estimated by the method of Lowry[10]. TCA was extracted from the supernatant by five successive washes with diethyl ether (four volumes). The sample was applied to a column of DEAE-'Sephadex' A25 (24 × 1.5 cm). A non-linear gradient was used for elution of adenine nucleotides. The gradient was formed in three equal chambers (500 ml each) containing respectively 0.02 M NH_4HCO_2, pH 4.8, 0.2 M NH_4HCO_2, pH 4.8, and 0.4 M NH_4HCO_2, pH 8.6. Fractions containing cyclic AMP were identified by the tritiated internal standard (Fig. 2). ATP was the major radioactive component eluted (60% of incorporated ^{14}C). The specific radioactivity of ATP was measured to compensate for twenty-five to thirty-fold dilution of labelled adenosine by endogenous pools of adenine nucleotides. The recovery of ATP and the ratio of ATP to ADP (12.5:1) indicated that breakdown of nucleotide phosphates during isolation had been minimal. The cyclic AMP recovered from the ion-exchange column was chromatographed twice on cellulose thin layers (0.5 mm) using first isopropanol and 0.03 M NH_4HCO_3, pH 8.6 (3:1 v/v), and then isopropanol, 0.1 M H_3BO_3 and saturated NH_4OH (7:2:1 v/v). Table 1 shows the recovery of ^{3}H and ^{14}C during the purification of cyclic AMP.

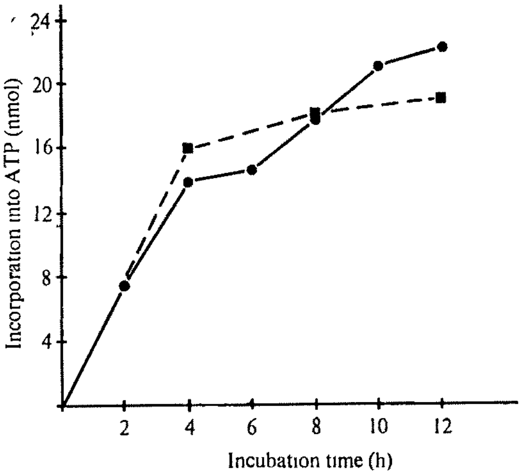

Fig. 1 Incorporation of adenosine into ATP by barley aleurone layers. Aleurone layers were isolated from barley seed (*Hordeum vulgare* L. cv. Himalaya) by the method of Chrispeels and Varner[8]. Sample layers were tested for sterility by incubation on nutrient agar. 100 layers were incubated at 25° C, with shaking, in groups of twenty layers per 50 ml Erlenmeyer flask containing 4 ml medium (1 mM NaOAc, pH 4.8, 20 mM $CaCl_2$). GA solution was sterilized by 'Millipore' filtration and was added to a final concentration of 10^{-6} M when appropriate. For determination of incorporation into ATP, 8-^{3}H-adenosine (15 × 10^6 c.p.m., 18.8 nmol) was included in each flask. Adenine nucleotides were isolated by grinding aleurone layers in ice cold 10% TCA, and analysed by ion-exchange chromatography. (●) Without GA, (■) with GA.

There is considerable enrichment of ^{3}H-internal standard with respect to incorporated ^{14}C at each stage of purification. This differential recovery of isotopes was not observed when authentic ^{14}C-cyclic AMP cochromatographed with ^{3}H-cyclic AMP. Clearly, most of the ^{14}C recovered at earlier stages during purification is not in the form of cyclic AMP.

The cyclic AMP from the second thin layer chromatography (TLC) step was recovered from scintillation fluid by adsorption on Whatman 3 MM paper (50 to 70% recovery). Paper electrophoresis was used as a fourth stage of purification (2.5 h at 20 V cm^{-1} in 0.06 M NH_4OAc, pH 3.5). Enrichment of ^{3}H-cyclic AMP with respect to ^{14}C was again observed (Table 2). It is doubtful therefore that the remaining ^{14}C recovered

Table 1 Incorporation of U-^{14}C-Adenosine and Recovery of Cyclic AMP in Barley Aleurone Layers

		Duration of GA treatment (h)					
	0	0.5	1	2	4	8	No GA
^{14}C-adenosine in medium (× 10^{-6})	104.6	104.0	103.2	105.3	103.5	100.0	96.1
^{14}C-uptake (× 10^{-6})	35.3	36.0	34.9	32.6	32.8	34.4	31.6
^{3}H-cyclic AMP added as standard	237,345	493,905	490,470	237,525	226,500	221,535	232,635
Cyclic AMP from ion-exchange ^{3}H	112,690	219,150	226,512	116,980	109,280	129,878	124,070
Cyclic AMP from ion-exchange ^{14}C	25,880	24,690	25,587	31,500	29,240	28,056	24,130
Cyclic AMP from first TLC ^{3}H	109,540	155,022	216,636	80,206	83,614	95,076	104,556
Cyclic AMP from first TLC ^{14}C	4,910	3,360	1,460	2,296	2,848	392	2,012
Cyclic AMP from second TLC ^{3}H	75,011	106,212	126,040	71,241	78,504	101,040	98,649
Cyclic AMP from second TLC ^{14}C	41.8	84.5	90.6	35.3	48.6	67.9	44.6

All incubations were for a total of 12 h, otherwise conditions were as for Fig. 1. GA was added for the periods indicated before termination of the incubation. All values are c.p.m.

Table 2 Recovery of Cyclic AMP after Electrophoresis, and Estimate of Possible Cyclic AMP Synthesis during the Incubation

	Duration of GA treatment (h)						
	0	0 5	1	2	4	8	No GA
^{3}H-cyclic AMP added as standard (c p m)	237,345	493,905	490,470	237,525	226,500	221,535	232,635
Cyclic AMP from electrophoresis (c p m) ^{3}H	43,317	53,010	81,782	28,963	30,227	40,597	39,672
Cyclic AMP from electrophoresis (c p m) ^{14}C*	12 4	5 9	16 1	7 2	7 8	11 5	9 7
Recovery (%)	18 2	10 7	16 7	12 2	13 4	18 3	17 1
Total ^{14}C in putative cyclic AMP (c p m)	67 9	54 6	95 6	58 8	58 1	62 6	56 9
Specific radioactivity of isolated ATP (c p m pmol^{-1})	32 1	33 0	27 5	30 7	29 3	34 8	26 2
Estimate of ^{14}C as cyclic AMP (pmol)	2 1	1 65	3 5	1 9	2 0	1 8	2 2

* Based on counts accumulated in 60 min, and after subtraction of 10 2 c p m background Additional background counts that did not originate from the adsorbed sample were eluted from electrophoresis paper The variability of contamination prevented estimation of individual errors, and the results reported remain uncorrected 3 to 6 c p m of the ^{14}C counts recovered after electrophoresis may originate by contamination from this source Eluates from unused electrophoresis paper contained similar high background counts

with cyclic AMP really represents incorporation of labelled precursor into the cyclic nucleotide Losses incurred, coupled with high background counts, prevented measurement of ^{14}C retention with the ^{3}H-cyclic AMP standard after further purification

With the above data, synthesis of cyclic AMP in barley aleurone layers seems unlikely, but cannot be disproved beyond the detection limits of this procedure The estimate of 2 to 3 pmol per 100 aleurone layers (1 5 g fresh weight or 75 mg protein) is best regarded as an upper limit for the possible presence of the cyclic nucleotide, a concentration one hundredth of that found in animal cells without hormonal stimulation[12,13] Also there is no sustained elevation of cyclic AMP synthesis resulting from treatment at a GA concentration (10^{-6} M) that induces the maximum amount of α-amylase[8] It seems unlikely that transient increases in cyclic AMP concentration could play a role in GA action, because the hormone must be continuously present to maintain α-amylase synthesis With GA at 10^{-6} M, an intracellular concentration of cyclic AMP no greater than 10^{-9} M would be inconsistent with the concept of the cyclic nucleotide operating as an amplification system for hormones[14] That cyclic AMP mediates the effects of GA in barley aleurone layers[3,5] must therefore be seriously doubted

Other evidence also suggests that analogies between the possible functions of cyclic nucleotides in higher plants and the system operating in animal cells are not reliable Cyclic nucleotide phosphodiesterase from pea seedlings[15] differs from the corresponding enzyme in animal cells[16] in its inability to discriminate between 2′,3′- and 3′,5′-cyclic nucleotides, by its product of hydrolysis, 3′-nucleotide, and by the failure of methylxanthines to inhibit its activity A similar enzyme is found in barley (P P C Lin, personal communication) My own work has shown that papaverine and the methylxanthines, theophylline and caffeine, do not retard the degradation of exogenously supplied ^{3}H-cyclic AMP by barley aleurone layers (unpublished observations) Inclusion of papaverine, theophylline or caffeine (each at 5 mM) in 12 h incubations of aleurone layers with ^{14}C-adenosine does not raise the recovery of ^{14}C with ^{3}H-cyclic AMP internal standard, using the procedures described here Protein kinases activated by cyclic nucleotides are widely distributed in animal tissues[17] The regulatory properties of cyclic nucleotides seem to result from their control of the phosphorylation of critical cellular proteins in such tissues[18] Protein kinases isolated from plant tissues are not activated *in vitro* by cyclic nucleotides (in preparation) Cyclic AMP is present in yeast[19], but is inactive on yeast protein kinase, and cyclic AMP-binding protein isolated from yeast has no protein kinase activity[20] Cyclic AMP levels in yeast are raised by glucose stress[19], a response similar to that in *Escherichia coli*[21] It seems likely that the role of the cyclic nucleotides in higher plants, if they do occur in these tissues, is quite distinct from their known functions in animal cells

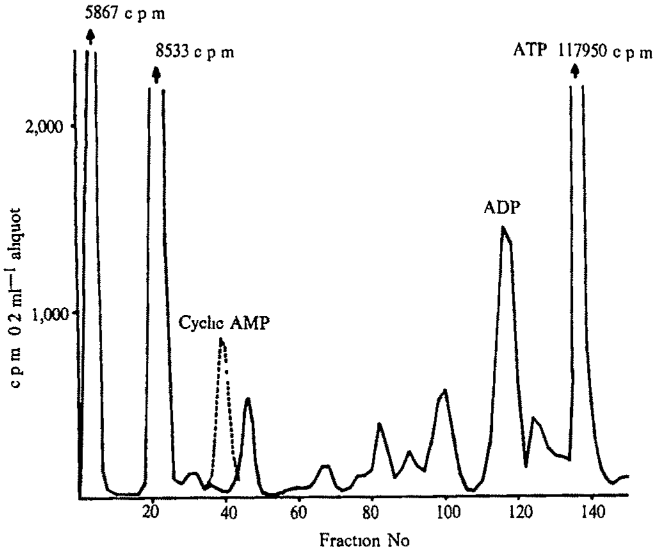

Fig 2 Elution of adenine nucleotides from DEAE-'Sephadex' A25 Radioactivity was determined in 0 2 ml aliquots from each 10 ml fraction, by liquid scintillation counting ATP was estimated by absorbance measurements at 260 and 290 nm (ref 11) on the peak fraction (fraction No 137 in this example) (——) ^{14}C, (- - -) ^{3}H

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Vitamin D-like Action of *Solanum malacoxylon* on Calcium Transport by Rat Intestine

A DISEASE of cattle, presenting gross symptoms of calcification of heart, lungs and other tissues, and known as *enteque seco* in Argentina or as *espichamento* in Brazil, has been shown to be due to the animals grazing a shrub, *Solanum malacoxylon*[1] Oral administration of the dried leaf of the plant can reproduce the symptoms of the disorder in cattle[2] In a study of calcium balance in cattle it was shown that oral dosing with the ground leaf could significantly reverse a negative calcium balance within a few days, the same workers concluded by use of a whole-body counting technique and tracer isotope that the increased retention of calcium was due to greater absorption rather than diminished calcium loss[3] The similarity of the clinical symptoms to vitamin D intoxication, taken along with these findings, suggests that the plant leaf may exert an effect on calcium absorption similar to that of vitamin D We report here a remarkable similarity in action of oral dosing of rats with *S malacoxylon* leaf and of vitamin D administration on the initial rates of uptake of calcium by intestinal mucosal preparations

The experiments were made on both normal and vitamin D-deficient animals Albino rats were weaned at about 50 g to either a normal (Oxoid 41B) or a modified Steenbock rachitogenic diet (Ca 1%, P 0 25%) At 3 weeks after weaning the normal animals had a mean weight of 140 g and the D-deficient animals 100 g On both the third and second days before experiment, four rats from each group were given orally 100–150 mg of ground leaf suspended in water Another four animals from each group were each given 50,000 IU of cholecalciferol (vitamin D$_3$) intraperitoneally 48 h before the experiment Three untreated control animals completed each dietary group Food but not water was withheld for 24 h from all animals before starting the experiments

The animals were decapitated and a segment of intestine, extending 6 cm distal to the pylorus, rapidly removed and mounted for measurement of the initial kinetics of calcium uptake across the mucosal surface, as has been described elsewhere[4] Conditions of incubation of the tissue were the same for all twenty-two rats, and the procedure is given in summary with Table 1 A calcium concentration of 1 0 mM was used, as in these conditions significant effects of vitamin D on initial kinetics of calcium uptake have been demonstrated[5]

Rats which had been on a normal diet responded to treatment with vitamin D (Table 1), the mean uptake being greater than in untreated controls at all three times of incubation The rates of Ca^{2+} uptake calculated were 1 11±0 22 and 1 93±0 23 nmol cm^{-2} min^{-1} for control and treated rats, respectively (means±s e) The dose of vitamin administered was large and this change in rate of Ca^{2+} uptake can be regarded as a maximum effect for this group of rats For similar rats given *S malacoxylon* leaf, the uptakes at 3 and 5 min were also significantly higher, at 1 min the value was higher than in the controls but this was not statistically significant Perhaps reflecting the smaller differences at each time of incubation, the rate of uptake in the *S malacoxylon*-treated animals was somewhat less than after vitamin D, but at 1 70±0 27 nmol cm^{-2} min^{-1} this was still substantially greater than for the control

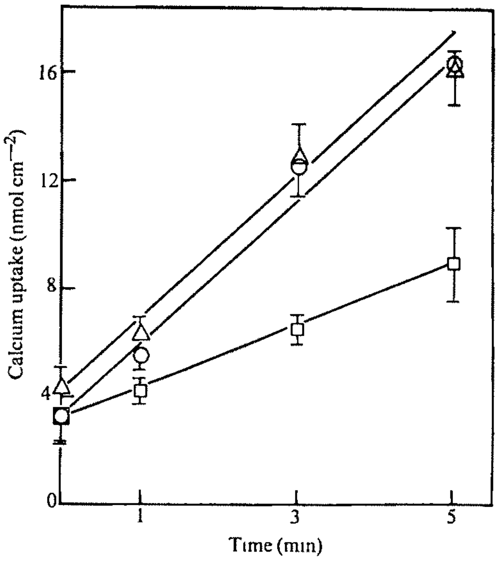

Fig. 1 Calcium uptake by the small intestine of rats raised on a diet deficient in vitamin D Conditions of the experiment are as described in Table 1 □, Control rats, ○, rats given 50,000 IU vitamin D$_3$ 48 h before experiment, △, rats given 100 mg of powdered *S malacoxylon* leaf 72 and 48 h before the experiment Points give mean values±s e of from six to twelve determinations, lines are generated assuming uptake to be linear with time from 1–5 min incubation

Table 1 Calcium Uptake by Intestinal Mucosa from Normal and Vitamin D-deficient Rats Treated with Vitamin D$_3$ or *Solanum malacoxylon* Leaf

Diet	Incubation (min) 1	2	3
Normal			
Control	3 33±0 33	5 85±0 60	7 78±0 91
D$_3$	5 17±0 27*	11 17±0 58*	12 89±0 85*
S malacoxylon	4 64±0 35	9 24±0 56†	11 37±1 01‡
D-deficient			
Control	4 20±0 59	6 50±0 53	9 02±1 39
D$_3$	5 55±0 53	12 51±1 17*	16 33±1 56*
S malacoxylon	6 34±0 61†	13 00±1 21*	16 20±0 68*

Numbers are mean calcium uptakes (±s e for six to twelve replicates) expressed as nmol Ca^{2+} cm^{-2} mucosal surface Statistical significance of difference from appropriate control, $P<0\ 001$ *, $P<0\ 01$ †, $P<0\ 05$ ‡ Segments of intestine were cut longitudinally and mounted so that the mucosal surface was bathed by phosphate-free, Tris-buffered physiological saline, oxygenated, at 37° C and *p*H 7 4 So mounted, a segment from one rat provided eight replicate areas of tissue each of 0 17 cm^2 and times of incubation were randomly distributed within each segment Calcium uptake was determined as ^{45}Ca activity in the tissue after incubation with medium containing a trace of ^{45}CaCl$_2$ Influx of Ca was terminated by a rapid wash with ice-cold, isosmotic mannitol The incubated tissue was stamped out of the intestinal strip, leached in dilute nitric acid and ^{45}Ca counted by liquid scintillation spectrometry A trace of ^{3}H labelled inulin was also in the medium and the tissue activity associated with inulin was deducted from the total tissue ^{45}Ca activity in order to compute calcium uptake into mucosal cells

Results for rats kept on a vitamin D-deficient diet are also shown in Table 1 Here the parallel between vitamin treatment and *S malacoxylon* treatment is striking At both 3 and 5 min incubation, highly significant increases, of similar magnitude, were obtained in both groups compared with controls The corresponding regression lines, calculated assuming uptake to be linear from 1 to 5 min incubation, are shown in Fig 1 The rate of uptake for vitamin D- and *S malacoxylon*-treated rat intestine was not different (2 70±0 26 nmol Ca^{2+} cm^{-2} min^{-1} and 2 47±0 24 respectively) and for control animals uptake was less than half this value (1 14 ± 0 33 nmol cm^{-2} min^{-1}) All regression lines gave positive intercepts on the ordinate This has been a consistent finding and has been attributed previously to a rapid initial uptake of Ca^{2+}, probably by non-specific adsorption to the microvillar surface[4,5] Treatment with vitamin D or *S malacoxylon* did not affect this rapid phase of Ca^{2+} uptake (3 22 ± 0 91 and 4 31 ± 0 83 nmol cm^{-2} for intestines taken from vitamin D- and *S malacoxylon*-treated rats compared with 3 27 ± 1 15 nmol cm^{-2} for controls)

Feeding the ground leaf of the plant can therefore elicit, within the same time, effects similar to vitamin D in normal rats and the effects of both vitamin D and leaf become more pronounced with rats kept on a rachitogenic diet Cholecalciferol (vitamin D_3) is known to require two successive hydroxylations, occurring in the liver[6] and kidney cortex[7], to yield the active metabolite, 1,25-dihydroxycholecalciferol, and it may be that the active principle of the plant has also to be metabolized before it produces its final effect Unlike the precursors of vitamin D, however, the active principle of *S malacoxylon* leaf is water-soluble[1] and this would seem to preclude its inclusion with the oil-soluble vitamins This water solubility might explain the ready extraction of the active material in the gut of different species, but the identity and mode of action remain unknown In this preliminary investigation, no attempt was made to determine an optimum dose or route of administration for the leaf Post-mortem examination showed clear traces of unabsorbed leaf material in the colon and one could assume, from the effects produced on Ca^{2+} absorption in the small intestine, that the amount of leaf administered was more than sufficient to elicit a maximum response

The present unequivocal demonstration that this particular species of solanaceous plant contains one or more active principles which closely resemble cholecalciferol in stimulating calcium absorption suggests a chemical similarity with known precursors of this vitamin, while its water solubility tends to deny such a relationship This apparent paradox can only be solved by the chemical identification of the active principle which should prove interesting as it might eventually find a clinical use and could give new insight into the general mechanism by which these types of compounds change calcium metabolism

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Mechanism for the Chromosome Banding Phenomenon

MAMMALIAN constitutive heterochromatin probably occurs in a variety of forms but chiefly two modes[1] These are (*a*) centromeric, which is found chiefly at the centromeres and paracentric constrictions, and (*b*) intercalary, which is found in other chromosomal regions Our experience with the banding techniques has led us to believe that the G bands (so called by a convention adopted by the Fourth Congress of Genetics, Paris, 1971) contain a considerable complement of intercalary constitutive heterochromatin We propose that it is chiefly this latter type of A–T rich constitutive heterochromatin that is enriched at the sites of the G bands, and that in the G banding techniques Giemsa stains the protein remaining at these sites after the various pretreatments

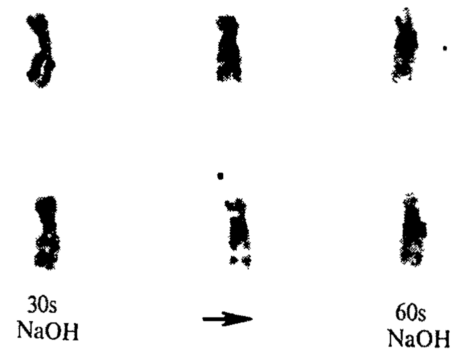

Fig. 1 Human No 9 Chromosome pairs from different metaphases subjected to different NaOH treatments The centre pair are G–C band hybrids Staining time with Giemsa is 3 min with 30 s NaOH treatment and 25 min with 60 s NaOH treatment

Reproducing the C band (by convention from the Fourth Congress of Genetics) technique of Arrighi and Hsu[2], we used varied times of NaOH treatment and Giemsa staining This produces a spectrum of banding patterns ranging from slides with chiefly G banded metaphases to slides with chiefly G/C band hybrids and then to slides with chiefly C banded metaphases, the last being produced with the longest treatment in NaOH (Fig 1) It is evident that the G bands are not quite as resistant to NaOH denaturation as the C bands The paracentric C bands in human chromosomes 1 and 16 also stain in the G band technique, however Further, the enormous blocks of constitutive heterochromatin on the sex chromosomes of the field vole (*Microtus agrestis*) do not stain as C bands in ignition spread preparation, but they do stain heavily in the G band techniques[3] Thus, the C band technique alone does not define constitutive heterochromatin clearly

Identical human G banding patterns have been produced with proteolytic enzyme preparations of different specificity[4–7] Differences in the nature of the protein are therefore not critical and access to the substrate may be more relevant Wilhelm *et al*[8] examined the histone and nonhistone proteins of both extra-nucleolar chromatin and nucleolar-associated chromatin (which is rich in heterochromatin[9,10]), and found that the striking structural differences between these two chromatin types were not reflected in their protein constitution There is some evidence, however, to suggest that heterochromatin-associated protein may have a low degree of phosphorylation[11,12]

Protein in densely packed heterochromatin would be more inaccessible to enzyme attack than that in euchromatic chromosomal regions It is probable that the more repetitive the DNA, the denser the packaging of the nucleoprotein Prolonged proteolysis completely removes the G bands and the chromosomes become swollen, non-staining structures which still contain abundant DNA, as shown by autoradiography, suggesting that Giemsa is a protein stain Many authors[13–17] have ascribed Giemsa banding to the denaturation and differential renaturation of DNA sequences It has been stated[14] that the darkly staining G banded regions represent a DNA component of the chromosome, but there is no evidence that this DNA is itself Giemsa stained In addition, although denaturation and renaturation of DNA occur in the banding methods using strong alkali treatment, these do not occur in those G banding methods using a neutral *p*H saline buffer or trypsin[18]

Synthetic DNAs rich in A–T base pairs strongly enhance the fluorescence of quinacrine and a corresponding quenching is seen with G–C rich molecules[19,20] Proflavine, an acridine related to quinacrine, gives similar banding results[21] In addition, the binding process of proflavine to DNA is similar, whether the chromatin is protein extracted with NaCl or not[22] This suggests that quinacrine fluorescence in chromosomes is due to the DNA composition and is unaffected by chromosomal protein

Comings[23] described families of sub-components of DNA in the Chinese hamster that tend to replicate at the same time He also described a return to A–T richness as heterochromatin is replicated late in the S period We believe that families of related sequences in fractions such as the "homogeneous main band DNA"[24] and the "intermediate reassociating repetitive DNA"[25] are prime candidates for localization in the intercalary constitutive heterochromatin of man Human homogeneous main band DNA is A–T rich[26] There is also some evidence in man that the intensely quinacrine-fluorescing bands are also late replicating[27,28]

Comings[29] postulated a mechanism (cytosine methylation and later deamination) whereby heterochromatic regions may evolve into A–T rich sites In the light of the above discussion, this mechanism would explain the similarities of the G and Q banding patterns We propose that G bands are found at sites enriched with types of constitutive heterochromatin correlating with Q bands only in so much as this heterochromatin is A–T rich The dissimilarities between the Q and G banding patterns are found at sites enriched with centromeric constitutive heterochromatin These could be explained by the presence of highly repetitive DNA which has not become A–T rich because of a high proportion of non-methylatable G–C base pairs in the original sequence which was amplified into the repetitive DNA

Our hypothesis of extraction of protein at differential rates seems to relate the results of the different banding techniques in man Table 1 shows the differing resistance to alkali disruption of various constitutively heterochromatic regions

Table 1 Differential Resistance of Constitutively Heterochromatic Regions to Alkali Disruption

		Time of alkali treatment →			
	Technique	ASG[14] trypsin[5]	Alkali/ saline[13]	C band method[2]	Giemsa 11[17]
	Regions				
Increasing resistance to treatment ↓	G bands	+	+		
	16 qh	+	+	+	
	1 qh	+	+	+	±
	Distal Yq		+	+	±
	9 qh			+	+
	Proximal Yp			±	+

+, Bands present, ±, bands sometimes present

The reverse banding technique[30] has its probable mechanism in the selective disruption of A–T rich sites at the specific temperature (87° C) of the prestaining treatment Protein in these disrupted areas would be more easily extracted than that at the more heat stable regions, which are relatively rich in G–C base pairs Again, a prolonged treatment produces non-staining structures A DNA sequence containing even 50% G–C base pairs would be relatively G–C rich, as compared with the A–T rich heterochromatin It is quite probable that the darkly staining R bands contain largely euchromatic DNA

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Androgen Metabolism in Rat Interstitial Tissue and Seminiferous Tubules

Although it is generally agreed that the interstitial (Leydig) cell of the testis is the main source of testosterone, which is essential for normal spermatogenesis, it has been suggested[1] that the seminiferous tubules may also be involved in steroid production

Evidence that the tubules are capable of metabolizing certain steroids has come from Christensen and Mason[2] and Hall *et al*[3] who have separated rat testicular tubules and interstitial tissue by dissection and demonstrated that both tissue fractions can convert pregnenolone and progesterone to androstenedione and testosterone *in vitro* Although the interstitial tissue was far more active than the seminiferous tubules (on a weight to weight basis) because tubules constitute the major portion of testicular mass, Christensen and Mason[2] concluded that as much as 10% of the testicular androgens may be produced in the seminiferous tubules

Hall *et al*[3] and Cooke *et al*[4] have failed to demonstrate cholesterol metabolism in rat seminiferous tubules but side chain cleavage of cholesterol by the tubules has recently been demonstrated by Bass *et al*[5] It seems that the seminiferous tubules are of minimal importance in the conversion of cholesterol to pregnenolone, but it is possible that pregnenolone enters the tubules[6] and is further metabolized there

In order to determine the role of the seminiferous tubules in the later stages of testosterone biosynthesis, we have studied the metabolism of dehydroepiandrosterone (DHA), an inter-

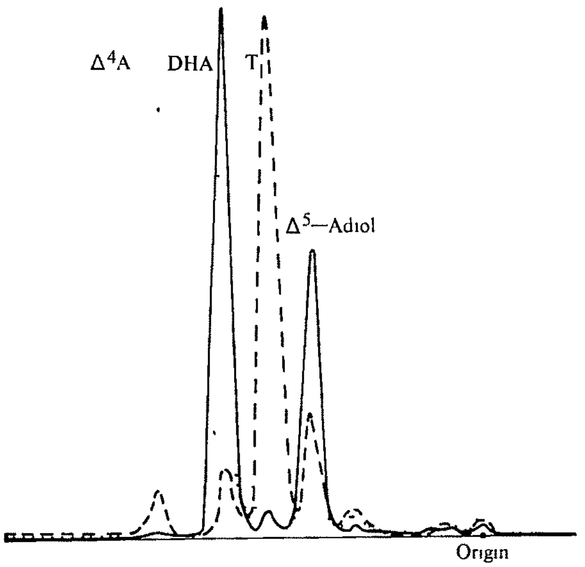

Fig. 1 Radiochromatogram scan of the metabolites formed from DHA-4-^{14}C *in vitro* by various fractions of the adult rat testis Thin layer chromatography was carried out on silica gel in dichloromethane acetone, 6 1 The plate was developed twice Δ^{4}A, Androstenedione, DHA, dehydroepiandrosterone, Δ^5-Adiol, androst-5-ene-3β,17β-diol, T, testosterone ——, Seminiferous tubules, , interstitial tissue, - - - whole testis

mediate on the 5-ene pathway of testosterone production, in isolated interstitial tissue and seminiferous tubules, as well as in the intact testis, from the adult rat Our results reaffirm the importance of the interstitial cell in androgen biosynthesis, but also reveal an important cooperative role of the tubules in determining the production of testosterone relative to other steroids

Tubules and interstitial tissue from one testis of a 6-month-old Sprague-Dawley rat (weight 640 g) were separated in medium 199 buffered with HEPES, following the method of Hall *et al*[3] The tubules were washed six times with fresh medium to remove any free cells, and were examined under the dissecting microscope to check that there was no gross interstitial cell contamination The interstitial tissue fraction contained short portions of tubules and free tubular cells Dissection of one testis by this method took 2 h The tunica was removed from the second testis, and the tissue kept in the same medium without dissection for 2 h The cell viability, checked with Leishman green stain, was found to be greater than 70% in the interstitial tissue, much of the dead material consisting of damaged tubules rather than interstitial cells Seminiferous tubules showed some uptake of the dye by peritubular cells where the tubules had been broken or damaged on dissection, but the cells extruding from the broken ends of tubules remained viable The undissected testis did not take up the dye Portions of each tissue fraction were processed for light microscopy when no contamination of the tubule fraction with interstitial cells could be seen

Each tissue fraction (tubules, interstitial tissue, and intact testicular tissue) was divided into two equal portions for incubation Thus, six flasks were set up, each containing tissue from half a testis After removal of the tunica, half a testis weighed 850 mg, the corresponding tubule fraction 740 mg, and the interstitial tissue fraction (with some tubular contamination) 90 mg

The contents of each flask were incubated for 2 h at 37° C with DHA-4-^{14}C (1 μCi, 16 nmol) in 8 ml medium 199 buffered with HEPES at *p*H 7 4, containing 15% foetal calf serum The reactions were stopped by adding dichloromethane The metabolites were investigated by the conventional techniques of thin layer chromatography, derivative formation and recrystallization to constant specific activity

The distribution of radioactivity after initial chromatography of lipid extracts from the incubations is shown in Fig 1 The four principal peaks of activity correspond to DHA (unreacted substrate), androst-5-ene-3β,17β-diol (androstenediol), androstenedione and testosterone (Fig 2) The identities of these peaks were confirmed by recrystallization, and the percentage conversion of substrate to products, in each incubation, is shown in Table 1

Table 1 Metabolism of DHA-4-^{14}C *in vitro* by Seminiferous Tubules, Interstitial Tissue and the Intact Testis from Adult Sprague-Dawley Rat

	DHA metabolized (%)					
Tissue type	ST	ST	INT	INT	W	W
Total metabolism	39 3	49 1	68 9	78 4	86 8	67 8
Androstenediol	36 7	45 9	5 8	5 1	11 5	11 6
Androstenedione	0 8	0 9	30 4	34 2	12 4	15 2
Testosterone	1 2	2 1	25 2	32 5	55 4	35 4
Unidentified metabolites	0 6	0 2	7 5	6 6	7 5	5 6

Each incubation contained the relevant tissue from half a testis
ST Seminiferous tubules, INT interstitial tissue, W intact testicular tissue, after removal of the tunica

The principal metabolite of DHA in adult rat seminiferous tubules is androstenediol, the production of androstenedione and testosterone is very low In contrast, in interstitial tissue, androstenedione and testosterone are the major metabolites, the production of androstenedione slightly exceeding that of testosterone In undissected testicular tissue androstenedione and testosterone are again the major metabolites, but the production of testosterone greatly exceeds that of androstenedione In addition, the production of androstenediol is greater than that found in interstitial tissue alone

These results demonstrate that the seminiferous tubules contain a high level of 17β-hydroxysteroid dehydrogenase, but a very low level of $C_{19}\Delta^5$-3β-hydroxysteroid dehydrogenase/isomerase activity The production of testosterone and androstenedione in the isolated tubules is only 4% of that in the corresponding interstitial tissue under the same conditions This low value cannot be accounted for by loss of tubules during dissection, or by damage to the tissue The cell type responsible for Δ^5-3β-hydroxysteroid dehydrogenase isomerase activity within the tubules is unknown, it has been suggested that the Sertoli cell is involved[1,2] Although the tubules appeared free of interstitial cell contamination when examined microscopically, the possibility of interstitial cell contamination cannot be completely ruled out

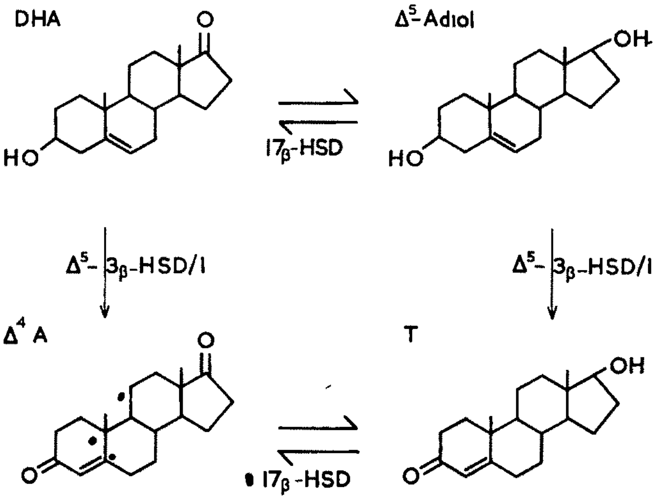

Fig. 2 The principal metabolites of DHA in the adult rat testis *in vitro* DHA, Dehydroepiandrosterone, Δ^5-Adiol, androst-5-ene-3β,17β-diol, Δ^{4}A, androstenedione, T, testosterone, 17β-HSD, 17β-hydroxysteroid dehydrogenase, Δ^5-3β-HSD/I, Δ^5-3β-hydroxysteroid dehydrogenase isomerase

Incubations with isolated tubules and undissected testis yielded testosterone to androstenedione ratios between 2 and 5. This is comparable to the ratios observed in spermatic venous blood of the adult rat[7]. The increased production of testosterone from DHA by undissected testis, compared with the isolated interstitial tissue, may be due to the high 17β-hydroxysteroid dehydrogenase activity within the seminiferous tubules.

These results confirm that the interstitial tissue of the testis is the principal site of conversion of 5-ene to 4-ene steroids. *In vitro* the seminiferous tubules have an important role in determining the relative production of androstenedione and testosterone. Whether the tubules have a similar role *in vivo* remains to be investigated.

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Methods of Examining Fibrinolysis in Plasma

IMMUNOLOGICAL methods have been used to estimate the levels of fibrinogen and fibrin degradation products in serum samples during thrombolytic therapy and in various clinical situations. A recent report[1] has suggested that methods such as the tanned red blood cell haemagglutination inhibition immunoassay[2] and latex aggregation[3] measure mainly the products of fibrin degradation. We wish to report on techniques which have proved useful in differentiating between the degradation products of fibrinogen and fibrin clots in whole plasma systems *in vitro* and which have helped in confirming results obtained[4,5] using purified fibrinogen and fibrin clots.

Human fibrinogen (Grade 4 from KABI AB, Stockholm) was used throughout these experiments and the human plasma used was freshly drawn into citrate from one of us (P. J. G.). Sodium dodecyl sulphate (SDS) acrylamide gel electrophoresis[6] was performed on reduced and unreduced protein solutions. The acrylamide gels were autoradiographed using a 15 h contact time with Osray-M X-ray film. To check the nature of the fragments released from clotted fibrin and plasma fibrinogen during enhanced fibrinolysis in plasma, 5 μCi of ^{125}I-labelled fibrinogen[7] was added to 1 ml of plasma and clotted with 2 NIH units of bovine thrombin (Diagnostic Reagents, Thame, Bucks.) for 30 min at 37° C. The radioactive plasma clot was wound on a wooden stick, washed with saline four times and placed in 1 ml of plasma. A second type of clotted fibrin was made by clotting 1 ml of a 0.3% fibrinogen solution (KABI Grade L) and 5 μCi of ^{125}I-labelled fibrinogen. This type of fibrin was also placed in 1 ml of plasma. One ml aliquots of ^{125}I-fibrinogen plasma were prepared with and without the two types of fibrin clots (non-radioactive). Sixty IU streptokinase (SK) in 20 μl of 0.15 M NaCl were added to all systems and incubated for 6 h at 37° C. A separate ^{125}I-fibrinogen plasma sample was treated with urokinase (UK) for 6 h at 37° C. Aliquot samples from each test system were electrophoresed on 5% SDS acrylamide gels (Fig. 1).

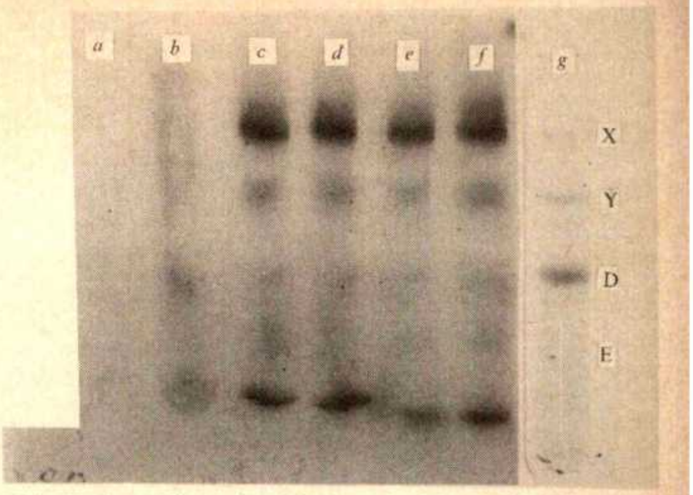

Fig. 1 Autoradiographs of SDS acrylamide gels (5%) showing the labelled fragments released from, *a*, ^{125}I-plasma clots in plasma by SK; *b*, ^{125}I-fibrin clots in plasma by SK; *c*, ^{125}I-plasma fibrinogen by SK in plasma containing plasma clots; *d*, ^{125}I-plasma fibrinogen by SK in plasma containing fibrin clots; *e*, ^{125}I-plasma fibrinogen by SK in plasma; and *f*, ^{125}I-plasma fibrinogen by UK in plasma; *g*, control group of reference fibrinogen fragments X, Y, D and E.

A control gel (Fig. 1*g*) shows the well characterized[8-12] groups of fibrinogen degradation products X, Y, D and E to which we wish to relate the fragments produced during degradation of fibrin clots and fibrinogen. During enhanced plasma fibrinolysis no radioactive material is released from the plasma clot while a clot made from purified fibrinogen releases low levels of a variety of compounds (Fig. 1*a*, *b*). Plasma fibrinogen in the presence of plasma clots and fibrin clots degrades mainly to a fragment similar in molecular weight to fragment X with lesser amounts of other components similar in size to Y, D and E (Fig. 1*c*, *d*). The concentration and range of degradation components are similar when ^{125}I-plasma fibrinogen is treated with SK and UK activated plasmin in the absence of clotted fibrin (Fig. 1*e* and *f*). Plasma fibrinogen, therefore, degrades mainly to fragment X and this reaction is not affected by the presence of fibrin clots.

It has been reported[13] that fibrin chain crosslinking catalysed by the plasma enzyme, Factor XIII, affects the susceptibility of fibrin to lysis with (UK). To assess why the plasma clot was less susceptible to lysis than the purified fibrin clot in plasma, both types of fibrin were examined for polypeptide chain composition before and after treatment with SK. The fibrins were washed in isotonic saline (0.2 M ε-aminocaproic acid (ε-ACA)) and treated overnight with 4 M urea (1% SDS 0.2 M β-mercaptoethanol) before electrophoresis in 7% SDS acrylamide gels (Fig. 2). A control mixture of the fibrin chains (α, β and γ, Fig. 2*e*) was used to relate the subunits in the test samples. It can be seen that the plasma clot (Fig. 2*a*) has all its γ chains crosslinked as γ-γ dimers and its α chains crosslinked to α polymers (α^p). Albumin chain impurities can be detected in the α chain region of the gels even after exhaustive washing of plasma clots[14]. The clot prepared from purified fibrinogen has some γ-γ dimers and no α polymers. The chain composition of the plasma clot after its attempted lysis with plasmin (Fig. 2*c*) is the same as that before lysis (Fig. 2*a*) while the partly crosslinked fibrin clot residue (Fig. 2*d*) is made up of β and some γ intact chains, γ-γ dimers and fragments of the α chain (α′, molecular weight, 25,000). These have been described elsewhere[15] as the initial α-chain residues which remain an integral part of non-solubilized fibrin.

Antiplasmins adsorbed into the totally crosslinked plasma clot might explain its resistance to lysis but thorough washing of these clots in saline reduces this possibility. We conclude that the presence of α-chain polymers, and to a lesser extent γ-γ chains, endowed these plasma clots with resistance to lysis (Fig. 1*a*) supporting recent subunit evidence[4] which rational-

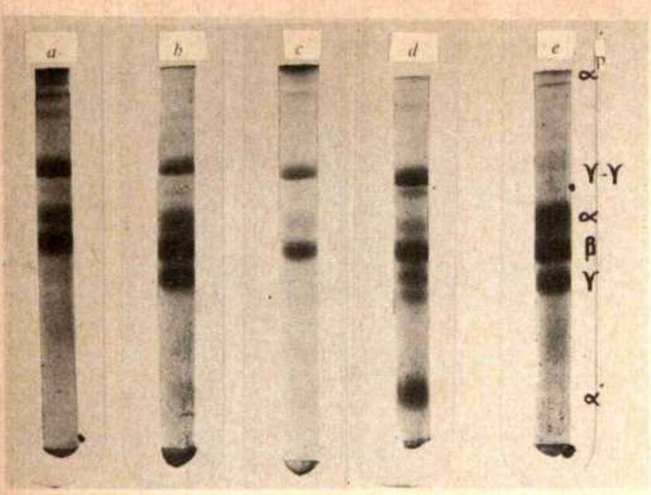

Fig. 2 SDS acrylamide gel (7.5%) electrophoretic patterns of the polypeptide chains of, *a*, totally crosslinked (TXL) plasma fibrin clots; *b*, partly crosslinked (PXL) purified fibrin clots; *c*, TXL plasma fibrin clots after SK activated fibrinolysis in plasma; and *d*, PXL purified fibrin clots after activated fibrinolysis in plasma; *e*, reference chains of fibrin α, β and γ whose molecular weights are 65,000, 56,000 and 47,000 respectively[15]. The plasma fibrin clots, (*a*) and (*c*), contain albumin impurity in the α chain location[14]. α-Chain polymers which cannot enter the gel (α^P); γ dimers (γ-γ); a fragment of the α chain of molecular weight about 25,000 (α′). Electrophoresis was for 15 h at 2 mA per gel, the gels were stained for 4 h in 1% Amidoblack and destained overnight with large volumes of 7% acetic acid.

izes the observation[16] that plasma clots produced in the presence of Ca^{2+} (necessary for Factor XIII activity and activation) are highly resistant to lysis by plasmin.

SDS acrylamide electrophoresis, autoradiography and immunoabsorption were used to examine the end products of the plasmin degradation of fibrinogen and fibrin in plasma. A ^{125}I-labelled plasma clot was treated in plasma with 60 IU SK and then five caseinolytic units of human plasminogen added, and incubated at 37° C for 4 h. An unlabelled clot was incubated in ^{125}I-fibrinogen plasma and treated similarly. The clots lysed rapidly and completely because of added plasminogen compared to the clots with no plasminogen added described above (Fig. 1). This supports the recent important role given[17] to plasminogen perfusion in clot lysis. Aliquots of the lysates were absorbed with rabbit anti-human fibrinogen serum and the washed immunoprecipitates were dissolved in 4 M urea (1% SDS), subjected to electrophoresis on SDS acrylamide gels and autoradiographed overnight (Fig. 3).

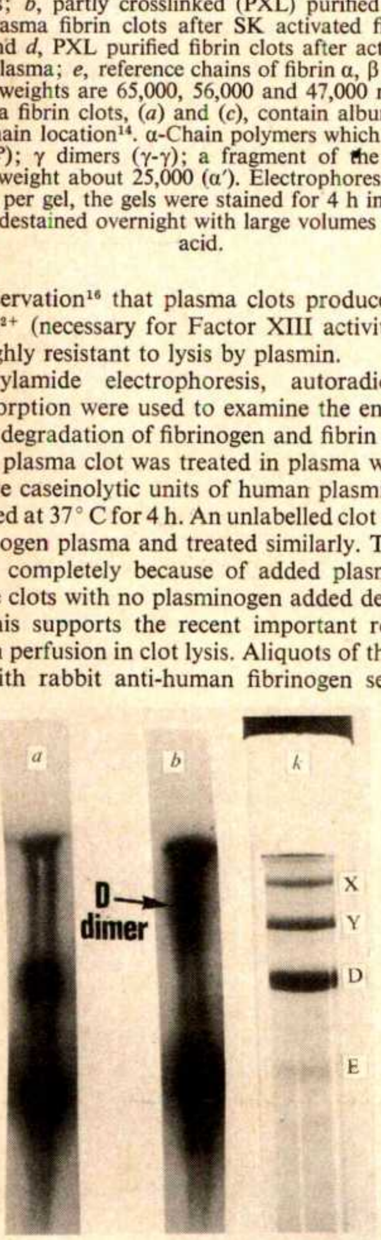

Fig. 3 Autoradiographs of SDS acrylamide electrophoresis gels (5%) showing the principal ^{125}I-labelled fragments absorbed by rabbit antihuman fibrinogen serum from plasminogen enriched SK treated: *a*, ^{125}I-plasma fibrinogen with non-labelled plasma clot; *b*, ^{125}I-plasma fibrin clot in non-labelled plasma. Pattern *k* shows the mobility of the known fibrinogen fragments X, Y, D and E for comparison.

The labelled fragments released from plasma fibrinogen (Fig. 3*a*) had the same mobility as fragments D and E in the control marker mixture (Fig. 3*k*) while those released from labelled clots (Fig. 3*b*) can be described as a dimerized form of fragment D and fragment E. These dimerized forms of D have been shown[4] to contain the γ-γ chain crosslinks of the originating fibrin clots. It seems that clotted fibrin does not release fragment D.

It is encouraging to realize that, in plasma, the use of SDS acrylamide gels coupled with the sensitive technique of autoradiography has helped us to confirm fibrinolysis findings[4,5] obtained in purified systems. Methodology to specifically measure levels of D dimer in plasma would be useful to monitor thrombolytic therapy and/or observe the clearance of *in vivo* fibrin deposits. We suggest that immunoabsorption of fragment D dimer from plasma may be useful as a concentration step as the dimer would be present at low levels in a blood volume of 5 l during the lysis of normal-sized thrombi.

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Unique Amyloid Protein Subunit common to Different Types of Amyloid Fibril

IT has been shown by Glenner *et al.*[1] that certain amyloid fibrils, chiefly derived from primary amyloidosis or amyloidosis associated with myelomatosis, consist of immunoglobulin chains or their fragments. The principal component of these fibrils seems to be derived from the variable part of monoclonal κ or λ light chains (Bence-Jones proteins). In addition, a "non-immunoglobulin" amyloid fibril protein with a molecular weight of 85,000, named by us protein AS (amyloid

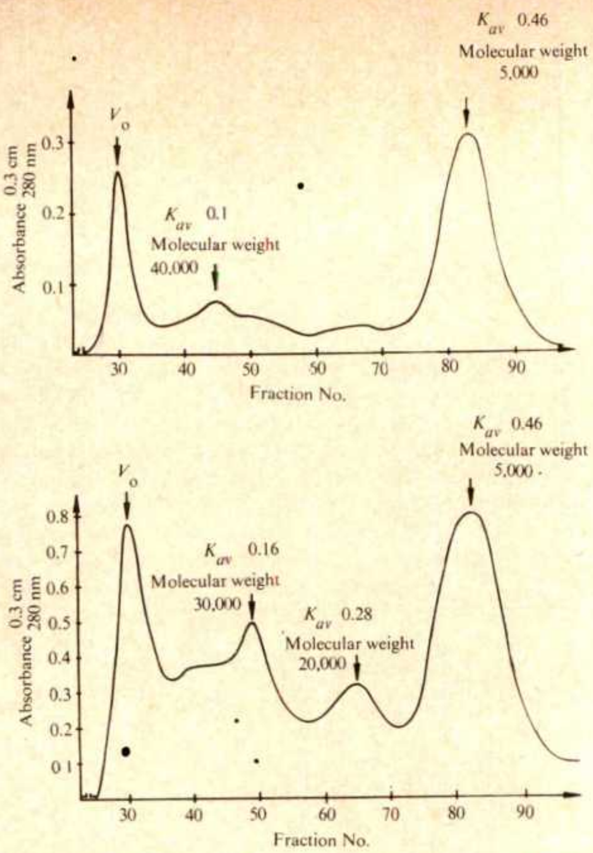

Fig. 1 Gel filtration of amyloid XVIII and amyloid XIII on a 3.2 × 96.5 cm 'Sephadex' G100 column with $V_0 = 157$ ml. Elution rate: 8.1 ml h^{-1}. Elution buffer: 5 M guanidine-1 N acetic acid; temperature: 23° C. Fraction volume 5.4 ml. Samples: amyloid XVIII: 10 ml, absorbance $^{1\,\mathrm{cm}}_{280\,\mathrm{nm}}$: 30; amyloid XIII: 15 ml, absorbance $^{1\,\mathrm{cm}}_{280\,\mathrm{nm}}$: 30.

subunit), which comprises an essential part of some secondary amyloid fibrils, has been detected by Benditt *et al.*[2] and by other groups[3-5]. The protein AS is found in secondary amyloid, chiefly associated with chronic inflammations, and has been suggested to be a fragment of a hitherto unknown larger protein[4]. Except for the detection of some light chain material connected with amyloid fibrils of the "non-immunoglobulin" type[6,7], no chemical link between the primary ("light chain") and secondary ("non-immunoglobulin") classes of amyloid substances has been established. On the contrary, the question has been raised whether there are two completely different chemical classes of amyloid[8].

We now report the first demonstration of protein AS in a patient with amyloidosis associated with Waldenström's macroglobulinaemia with typical serum IgM M-components and Bence-Jones proteinuria and in other cases classified as primary amyloidosis. Furthermore, a serum component antigenically related to the amyloid protein AS was detected both in patients with secondary amyloidosis and also in several cases of primary or myeloma/macroglobulinaemia associated amyloidosis. The findings indicate that the protein AS may be a unique common constituent of amyloid.

The study included two males, J. B., 67 yr, and J. N., 62 yr, who had typical Waldenström's macroglobulinaemia with progressing anaemia and lymph node enlargement and massive infiltration of lymphoid cells in bone marrow and lymphoid tissue. Monoclonal IgM in one patient (J. B.) 22 mg ml^{-1} of κ type, in the other (J. N.) 64 mg ml^{-1} of λ type, was found in serum, and both patients had significant Bence-Jones proteinuria with κ and λ light chains respectively. One patient (J. B.) developed generalized amyloidosis and died in uraemia. At autopsy, massive amyloidosis was found in bone marrow, lymphoid tissue and various parenchymal organs. The liver (3,800 g) consisted of 80% amyloid, as estimated on the basis of Congo red positive material in tissue sections, and was chosen for preparation of amyloid fibrils (amyloid XVIII). From the other patient (J. N.) enlarged lymph nodes were removed from the axilla by surgery and used as source for amyloid fibrils (amyloid XIX). Amyloid from some other cases of primary amyloidosis and eight cases of secondary amyloidosis was also studied. All available sera from patients with amyloidosis and several from other disease groups were also studied.

Amyloid fibril suspensions were prepared according to Pras *et al.*[9] and treated with guanidine or sodium hydroxide followed by gel filtration on 'Sephadex' G100 and G25 as previously described[7,10]. Antiserum was obtained by immunizing rabbits with crude alkali-treated amyloid (DAM)[7]. Amino acid composition and partial N-terminal amino acid sequence analysis by Edman degradation was performed as described by Husby *et al.*[10].

In all eight instances so far studied, degraded amyloid from secondary amyloidosis showed a consistent and typical elution pattern (Fig. 1) (amyloid XIII). This pattern was different in some of the primary amyloidosis cases studied, which in particular lacked the pronounced last peak, where the non-immunoglobulin protein AS was found in secondary amyloid. The gel filtration pattern of guanidine treated amyloid XVIII from the Waldenström's macroglobulinaemia case J. B. was, however, very similar to that of secondary amyloid XIII (Fig. 1). A distinct peak was eluted at K_{av} 0.46, which is exactly where the non-immunoglobulin protein AS was eluted in the cases of secondary amyloidosis.

Antigenic identity was also demonstrated when crude DAM or purified protein AS of amyloid I, derived from a patient with amyloidosis secondary to juvenile rheumatoid arthritis[7] and amyloid XVIII, was tested in double immunodiffusion against anti-DAM I or anti-DAM XVIII. Crude DAM gave two precipitation lines, while protein AS showed one line fusing with that of the crude DAM appearing closer to the antiserum well (Fig. 2*a*).

The amino acid composition of material eluted with K_{av} 0.46 of amyloid XVIII (J. B., Table 1) was very similar to that of secondary amyloid I. Furthermore the five N-terminal amino acids were Arg-Ser-Phe-Phe-Ser, which are identical to the corresponding N-terminal amino acids of protein AS of secondary amyloid I. Thus, by gel filtration, immunodiffusion experiments, amino acid composition and N-terminal sequence analysis, amyloid XVIII from Waldenström's macroglobulinaemia was shown to contain significant amounts of protein AS, which was similar to that of secondary amyloidosis.

When DAM from the other Waldenström patient (J. N., amyloid XIX) and from two other cases (amyloid III and VII) of primary amyloidosis were tested antigenically, a precipitation line which fused with that of protein AS was obtained, demonstrating protein AS-like material in these preparations. In two cases (amyloid XIX and amyloid VII from a case of primary amyloidosis) no protein AS was eluted at K_{av} 0.46 from

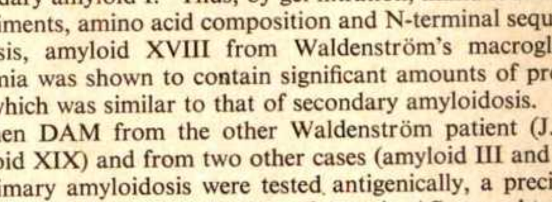

Fig. 2 *a*, Anti-DAM in central well tested against DAM I (1), DAM XVIII (2), protein AS XVIII (3), and protein AS I (6). The other wells (4 and 5) were filled with saline. Stained with amido black. *b*, Anti-protein AS in central well tested against DAM XVIII (1), serum from a case with secondary amyloidosis (2), DAM XIX (3), serum J. B. (4), protein AS I (5), and serum J. N. (6).

Table 1 Amino Acid Composition of Protein AS

	Residues per 100 residues	
	XVIII	I
Asp	13.3	13.8
Thr	0.74	0.44
Ser	6.96	7.06
Glu	8.55	8.42
Pro	2.02	1.64
Gly	11.3	11.9
Ala	16.4	15.9
Cys/2*	0.4	0.37
Val	1.73	1.45
Met	3.02	2.80
Ile	3.72	3.81
Leu	2.57	2.08
Tyr	5.69	5.50
Phe	7.96	8.86
His	2.03	2.59
Lys	3.41	2.91
Arg	10.2	10.9

Tryptophan was not determined.
* Cys/2 was determined as cysteic acid after performic acid oxidation.

guanidine treated material. Such material could be released and was eluted at K_{av} 0.46, however, after treatment of the amyloid with sodium hydroxide. Thus protein AS was demonstrated in several cases of so-called primary or myeloma/macroglobulinaemia associated amyloidoses.

With several good antisera available to detect the two principal components of amyloid, a search for amyloid-like material in human sera was attempted. One antiserum in particular (anti-DAM XVIII) reacting chiefly with protein AS gave a specific precipitation line with many human sera, particularly those of amyloidosis patients. These lines fused with that obtained with purified protein AS from amyloid fibril preparation (Fig. 2*b*). The precipitation reactions could also be blocked by adding purified protein AS to the antiserum. The positive sera came from various groups of patients (Table 2). These included sera of thirty-nine out of forty-one patients with amyloidosis amongst which were the two Waldenström's macroglobulinaemia cases, J. B. and J. N., in addition to patients with amyloidosis associated with myelomatosis and various conditions classified as either primary or secondary amyloidosis. A serum component related to protein AS has thus been found both in patients with primary and secondary amyloidosis. Several patients with diseases frequently complicated by amyloidosis were also positive. In contrast, isolated myeloma proteins, Bence-Jones proteins and normal sera were negative, except for a weak positive reaction in a single normal serum. It is, however, possible that protein AS is present in very small amounts, not detectable by our methods, in normal sera.

Table 2 Presence of Protein AS-related Serum Component

Diagnosis	No. positive/No. tested	
	Total	With known amyloidosis
Primary amyloidosis	7/7	7/7
Myelomatosis	47/88	3/4*
Macroglobulinaemia Waldenström	8/8	3/3
Rheumatoid arthritis	25/46	8/9*
Juvenile rheumatoid arthritis	20/38	8/8
Systemic lupus erythematosus	5/23	—
Cirrhosis of the liver	15/41	1/1
Ulcerative colitis	3/4	3/3
Familial Mediterranean fever	1/1	1/1
Cystic fibrosis of the pancreas	1/1	1/1
Medullary carcinoma of the thyroid	1/1	1/1
Other malignant diseases	3/3	3/3
Normal controls	1/70	—

* Patients with amyloidosis without protein AS-related serum component had severe liver and kidney conditions with hypoproteinaemia.

Testing of positive sera after gel filtration ('Sephadex' G150) showed that the molecular weight of the protein AS related serum component is approximately 100,000, and immunoelectrophoresis of the sera against anti-DAM revealed an electrophoretic mobility in the α–β globulin region.

The amyloid fibril protein AS thus seems to be more widely distributed among different amyloid substances than thought originally and is not restricted to amyloidosis associated with inflammatory conditions. The classification of amyloid fibrils into an immunoglobulin (light chain) type related to primary or myeloma/macroglobulinaemia associated amyloidosis and a non-immunoglobulin type related to secondary amyloidosis is therefore not consistent in all cases. While protein AS was always found in secondary amyloidosis, this protein on several occasions also appeared in primary or myeloma/macroglobulinaemia associated amyloidosis, either directly in the amyloid substance or as a protein AS-related component in the serum. Thus protein AS may be a unique component common to different types of amyloidosis. The detection of protein AS in the serum of the vast majority of patients with amyloidosis may prove to be a valuable diagnostic tool in amyloidosis and possibly enable us to detect the precursor state of this serious disease.

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Trypanosome Identification by Electrophoresis of Soluble Enzymes

IT is now generally accepted that interspecific differences are the result of inherited variations, developed during the course of evolution, in the structures (and amounts) of the proteins of the species concerned. Thus, although organisms of many diverse types possess cytochrome *c*, the cytochrome *c* molecules differ in structure, from organism to organism, to an extent which is related to the time that has elapsed since divergence from a common ancestor[1], and the same is true for the haemoglobins of animals[2]. Intraspecies differences are the outward manifestations of less profound modifications affecting only a few of the proteins. Thus some human racial groups differ in the incidence of certain of the variant forms of plasma proteins and red cell enzymes, and also in the incidence of some of the blood group types (which are now recognized as resulting from the activities of variant enzymes)[3]. Clearly, if analogous proteins in different strains of a species could be characterized in some way, such as by electrophoresis, which shows up small structural differences, biochemical classification of the different strains would be possible, and this could be of some value as a taxonomic tool. Some advances along these lines have already been made: in the field of protozoology for instance, different strains as well as different species of the malarial parasite were recently reported to differ, to a lesser and greater degree respectively, in electrophoretic characteristics[4].

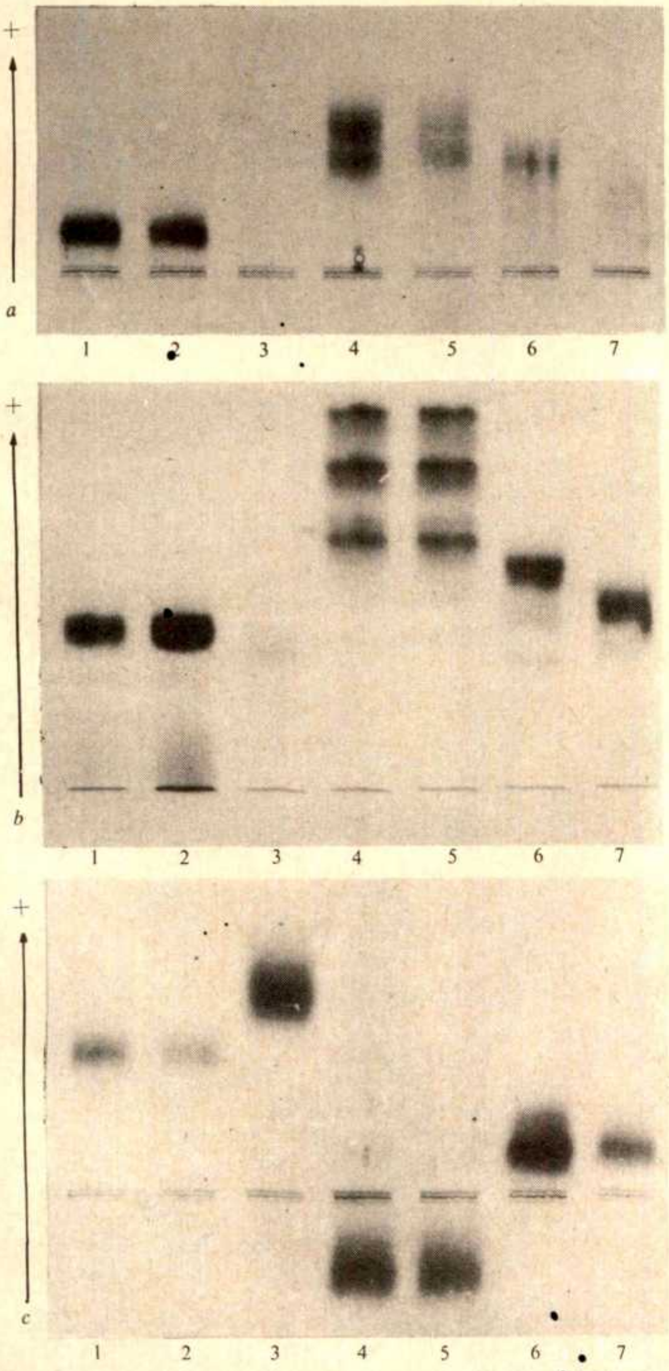

Fig. 1 Starch-gel electrophoretic patterns for seven different trypanosomal soluble extracts. A potential gradient of 15 V cm^{-1} of gel length was used, for a period of 4 h. *a*, Stained for G6PD; *b*, for ME; *c*, for PGI. Positions: 1, *T. lewisi* (Winches II); 2, *T. lewisi* (Molteno B$_3$); 3, *T. congolense* (1/148) (recently transmitted by tsetse fly); 4, *T. vivax* (Liverpool Swain strain); 5, *T. vivax* (Desowitz strain); 6, *T. b. brucei* (8/18) (recently transmitted by tsetse fly); 7, *T. b. brucei* (Ob$_2$).

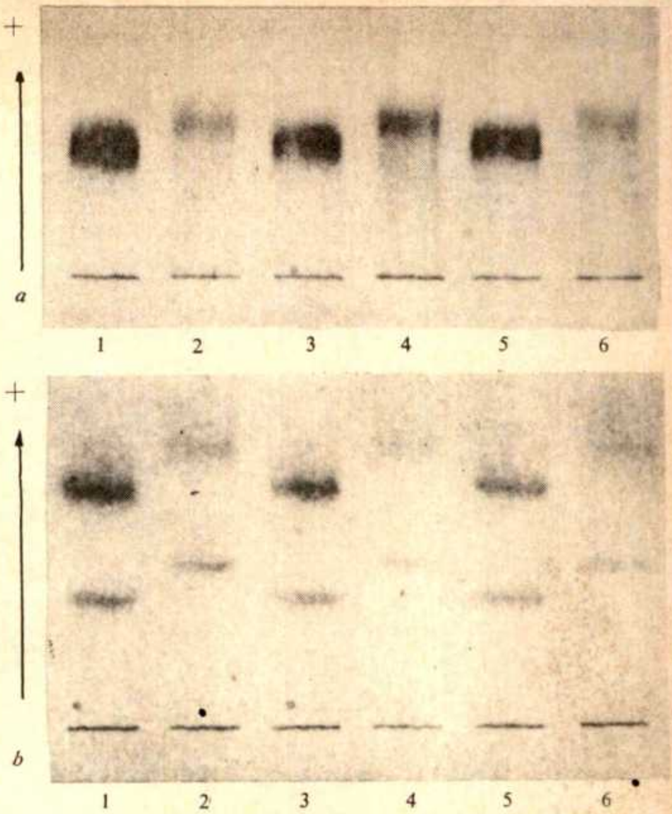

Fig. 2 Starch-gel electrophoretic patterns for soluble extracts from a *T. b. brucei* strain and a *T. b. rhodesiense* strain. A potential difference of 15 V cm^{-1} of gel length was used, for a time of 4 h. *a*, Stained for G6PD; *b*, for ME. Positions: 1, 3 and 5, *T. b. brucei* (Ob$_2$); 2, 4 and 6, *T. b. rhodesiense* (21).

We report here some well-defined differences in the electrophoretic behaviour of three soluble enzymes derived from four different trypanosome species, and some less well-defined differences between strains from within those species. This report, together with that of Kilgour[5] on trypanosome aminotransferases, suggests that a systematic study of enzyme electrophoretic mobilities and relative activities will yield a new procedure for the identification of the different trypanosome species and possibly also for the identification of different strains.

Soluble extracts[5] from some long term laboratory trypanosome strains were subjected to horizontal thin-layer starch-gel electrophoresis by a procedure essentially as described by Wraxall and Culliford[6]. The gels were then specifically stained for glucose-6-phosphate dehydrogenase (G6PD), the NADP-linked decarboxylating malic enzyme (ME), and phosphoglucose isomerase (PGI). G6PD was visualized by a procedure[7] whereby the gel was incubated with glucose-6-phosphate, NADP, phenazine methosulphate (PMS) and the tetrazolium salt MTT: the NADPH$_2$ formed by the enzymatic reaction, in the presence of the hydrogen carrier PMS, reduced the MTT to a deep blue insoluble formazan which deposited at the sites of G6PD activity. ME was stained by a parallel procedure: the gel was incubated with a mixture containing malate, NADP, PMS and MTT: the blue formazan precipitated at the sites of ME activity. PGI was visualized by incubation with fructose-6-phosphate, added commercial G6PD, NADP, PMS and MTT: glucose-6-phosphate was first formed at the sites of PGI activity: it then reacted with the NADP in the presence of the added G6PD to form NADPH$_2$ which, using PMS, reduced the MTT to its deep blue insoluble derivative[8].

From the results shown in Fig. 1 the four trypanosome species *Trypanosoma lewisi*, *T. congolense*, *T. vivax* and *T. brucei brucei* differ from each other quite clearly in the electrophoretic behaviour of the three enzymes reported.

Some differences in levels of enzymatic activity are also very apparent from Fig. 1: *T. congolense* is characterized by a relatively high PGI activity and an almost absent G6PD and ME. As would be expected, differences between strains of the same species were not generally so evident, but differences in the ME mobilities of two *T. b. brucei* strains are shown in Fig. 1*b* (positions 6 and 7). Small differences were observed in both the ME and the G6PD electrophoretic mobilities when a *T. b. brucei* strain and a *T. b. rhodesiense* strain were run alongside each other (Fig. 2*a*, *b*).

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Photomicrography of Corneal Endothelial Cells *in vivo*

WE have described the principles of operation for a microscope designed to examine objects embedded in highly reflecting or scattering biological materials[1]. We present here the first successful application of this device to the observation of endothelial cells lining the inside of the cornea.

The corneal endothelium is of crucial importance in maintaining the transparency of the cornea[2]. Observation of corneal endothelial cells *in vivo*, using a slit-lamp microscope, began about 1920 (ref. 3), and is now a well established art. But useful magnification is typically limited to a maximum of about ×80, though in practice magnifications are usually considerably below this maximum[2]. For research purposes in particular, it is desirable to observe and to photograph corneal endothelial cells at higher magnifications than can be obtained with standard slit-lamp microscopy. For this reason, Maurice[4] developed a split-objective microscope for observing functioning endothelial cells at magnifications of around ×500. For most convenient operation and focusing of Maurice's microscope at the highest magnifications, it is necessary to make physical contact between the epithelial surface of the cornea and the objective, either through a coverglass or a liquid medium. Maurice and his colleagues have photographed functioning corneal endothelial cells in enucleated, intact eyes[4,5]. Using our microscope, we have been able to repeat and to extend these observations, observing individual corneal endothelial cells and some of their organelles at high magnifications in the eyes of living bullfrogs, for periods of more than 30 min. Observations were made without physical contact between the objective and the eye.

The optics of our laser microscope are so designed that at any instant, light reflected from only one point within the object is transmitted to a photomultiplier[6]. The amplified output of the photomultiplier intensity-modulates the electron beam of an oscilloscope. By scanning the laser beam with the objective lens, and scanning the intensity-modulated electron beam in synchrony with the objective lens, a two-dimensional image is displayed on the oscilloscope of the reflectivities of points lying within an object at a given fixed depth.

The objective lens we have found most satisfactory is a Zeiss LD-Epiplan lens, ×40, NA 0.60, with a working distance of 3.1 mm. We have used a continuous wave 5 mW He-Ne laser with a wavelength of 0.6328 μm. Only about a tenth of the laser output was necessary for observation of the endothelial cells. The levels of light at the cornea (and at the retina) during our examination of the corneal endothelium were well below threshold for damage to these tissues[7-9].

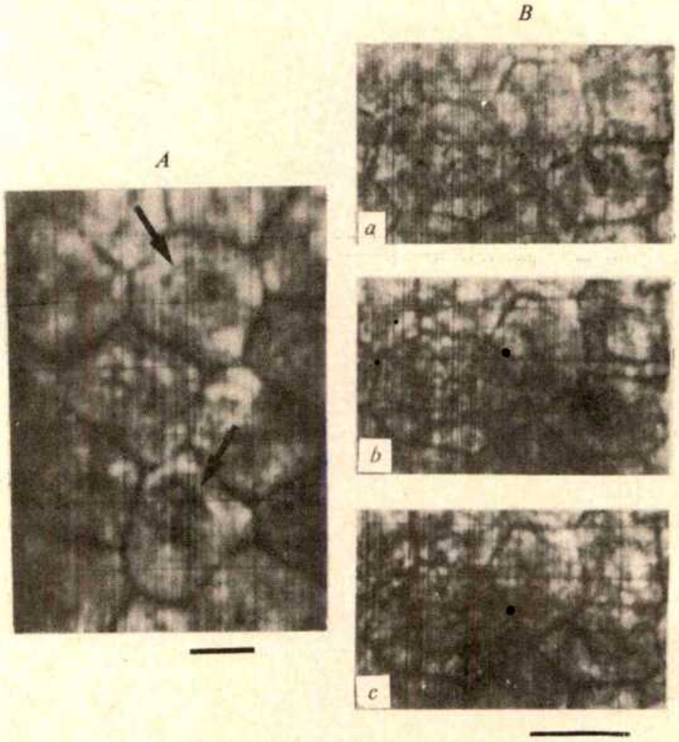

Fig. 1 *A*, Corneal endothelial cells in an unstained, unfixed intact eye of a living bullfrog. Arrows indicate outlines of the nuclei in two of the cells. Calibration mark, 25 μm. *B*, Three photographs of a group of corneal endothelial cells in an unstained, intact eye of a living bullfrog. *b*, Taken 15 min after *a*; *c*, taken 23 min after *a*. Calibration mark, 50 μm.

Figure 1*A*, which is a reproduction of a 'Polaroid' photograph of an oscillographic display, shows corneal endothelial cells within the eye of a living bullfrog, *Rana catesbeiana*. The bullfrog was immobilized by removing its brain and spinal cord. It was possible to observe a vigorous flow of blood in the vessels of the iris, both before and after this photograph was taken. Outlines corresponding to the nuclei of some of the endothelial cells are visible (arrows).

Figure 1*B* shows a series of three photographs of a group of corneal endothelial cells taken in another living bullfrog. The second picture (*b*) was taken 15 min after the first (*a*); the third (*c*), 23 min after the first. No gross differences in the arrangement or morphology of these cells or their nuclei occurred during this period.

We found, however, that in intact bullfrog eyes cooled to 4° C, sharp outlines of corneal endothelial cells, as seen in Fig. 1*A* and *B*, cannot be observed. Instead, only ghosts of outlines are seen, seemingly masked by highly reflecting regions at or near the plane of the endothelial cells. Whether these highly reflecting regions relate to changes in the morphology of the corneal endothelial cells themselves, or, perhaps, to changes in the hydration of Descemet's membrane immediately in front of the endothelial cell layer, is not known. These changes are, however, reversible and, as the eye warms to room temperature, the usual configuration of the corneal endothelial cells can be seen after warming for about 30 min These changes may be related to electrical and ionic events associated with decreased light transmission in cooled corneas[10]

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Further Investigations into the Teratogenic Potential of Imperfect Potatoes

IN a preliminary report[1] on the effects of feeding a dietary supplement of "blighted" potato concentrate to pregnant marmosets (*Callithrix jacchus*) reference was made to further experiments then in progress The results of these supplementary experiments are now available

The potatoes used in the experiments which form the substance of this report were all prepared and fed under identical conditions to those employed in the original "blighted" potato trial previously reported[1] The varieties used were normal domestic potato, potatoes rejected by graders in the food-processing industry (these were blighted, damaged and discoloured in the ratio 3 2 1) and tubers infected in the laboratory with *Erwinia carotovora*, a rotting organism known to produce rishitin and phytuberin in the tubers The results of this experiment are recorded in Table 1 While the offspring of both "domestic" and "reject" potato groups proceeded to term, those in the "*Erwinia*" group were obtained by hysterotomy to prevent the loss by parental destruction of any foetus born with gross anomalies No gross anomalies were found in any group, but behavioural defects comprising excessive clinging, abnormal play patterns, and inability to wean by 4 months were observed in three sets of twins born to mothers all fed with batch 1 of the "reject" potato concentrate These abnormalities of behaviour have not previously been observed in colony-bred marmosets

Terpenoid derivatives such as rishitin and phytuberin, and steroid glycoalkaloids including solanine, have been implicated in a hypothesis concerning the occurrence of spina bifida and anencephaly in man[2] In view of this and the results of the previous animal experiment[1], all samples involved in the present and earlier trials were analysed for total glycoalkaloids by accepted methods[3,4], for terpenoids by gas chromatography[5] and chloroform extracts were compared by thin layer chromatography (Table 2)

Table 2 Analysis of Potato Samples for Rishitin, Phytuberin and Total Glycoalkaloid Content in μg g^{-1} Freeze Dried Material

Sample	Rishitin	Phytuberin	Total glycoalkaloids
Kerr's Pink "blighted"	Trace	None	20
Erwinia-infected, batch 1	89	69	1
Erwinia-infected, batch 2	56	88	2
Industry-reject, batch 1	8	Trace	38
Industry-reject, batch 2	5	1	9
Industry-reject, batch 3	None	None	3
Domestic controls, batch 1	Trace	None	10
Domestic controls, batch 2	None	Trace	14

Although the levels of glycoalkaloids in Kerr's Pink "blighted" potato concentrate were higher than in the controls, it is unlikely that this difference alone is significant in relation to the cranial defects observed in the earlier experiment as higher levels in the "reject" batch I mentioned did not produce the same effect Rishitin and phytuberin, though present at high levels in the "*Erwinia*" concentrate, produced no malformations comparable with the cranial osseous defects previously observed

To check the possibility that organic mercury might be involved in the production of cranial defects[6] analysis of the mercury content was carried out The highest level, in Kerr's Pink potato concentrate, was 0 004 mg kg^{-1} fresh weight, and just within the normal range

Shepard[7] suggested that cytochalasin, which had been implicated in neural tube malformations in chick embryos[8], may be present in blighted potato Analysis of all samples for cytochalasin activity by Carter (personal communication) revealed no activity in any sample except for the original Kerr's Pink potato concentrate A weak but typical effect (binucleation in cultured L cells[9]) was found, representing a total daily dose per marmoset in the original trial[1] equivalent in activity to 3 μg of cytochalasin B The source of this activity could have been fungal pathogens such as *Phoma exigua* and *Helminthosporium solani*, known cytochalasin producers, found in mouldy seed potatoes[10]

Table 1 Comparison of Offspring in Potato Feeding Trials

	"Domestic" potato Group 1	"Industry reject" potato Group 2	*Erwinia* potato Group 3
No of treated females	6	7	5
Offspring this pregnancy	10 (4×2, 2×1)	12 (5×2, 2×1)	13 (3×3, 2×2)
Sexes this pregnancy	Seven males, three females	Six males, six females	Seven males, six females
Offspring previous pregnancy	11 (5×2, 1×1)	12 (5×2, 2×1)	11 (4×2, 1×3)
Sex previous pregnancy	Six males, five females	Six males, six females	Six females, five males
Gross anatomical defects	0	0	0
Behavioural irregularities	0	6 (3×2)	Not examined

The significance of the behavioural abnormalities cannot be assessed in full until the animals have been observed to develop to sexual maturity The higher levels of glycoalkaloids in the "reject" batch 1 fed to these mothers may be of significance solanine is toxic to man[11] but not apparently teratogenic in the rat[12]

The only safe conclusion that can be drawn from these supplementary experiments is that the cranial defects were not reproduced. Some correlations can be made between the chloroform extract analyses obtained by thin layer chromatography. Components, as yet unidentified, but common to both the original "blighted" potato and the present industry reject samples, were found , the significance of this remains to be established Parameters for assessing the behavioural effects of teratogens have yet to be defined Obviously such studies will play an increasing role in teratological testing in the future for, as has recently been stated, "the social and political implications of such a situation are enormous"[13]

Additional studies are in progress to re-examine Kerr's Pink blighted potato, and the effects of cytochalasin and solanine on marmoset morphogenesis

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Radiation Sterilization of *Aedes aegypti* in Nitrogen and Implications for Sterile Male Technique

ONE of the problems that often arise with mosquitoes and other insects when radiation-induced dominant lethality (sterile-male technique) is used is that sterilized males cannot compete with untreated native males for matings with females It is generally believed that the field trials of releases of radiation-sterilized males of *Aedes aegypti* in the United States were unsuccessful because radiation impaired vigour and competitive mating ability of released males[1] In the case of *Aedes aegypti*, these conclusions were experimentally confirmed by Weidhaas and Schmidt[2] Adults emerged from male pupae irradiated at 8,000 and 10,000 r inseminated only 4 and 0% of the females respectively when released into laboratory populations at a ratio of four treated males to one untreated

It has been observed that the effects of irradiation on living organisms may be modified by changing the internal environment of the cell experimentally Thoday and Read[3] decreased the oxygen concentration in irradiated *Vicia faba* and found a lower mutation frequency Hollander, Baker and Anderson[4], in a study of the mutation rate of sex-linked lethals induced by irradiation in male *Drosophila melanogaster*, found the mutation rate to vary from 8 to 16% correlative with increased oxygen concentration Baldwin and Chance[5] reported on the improved competitiveness of males of *Rhodnius prolixus* sterilized by irradiation in the absence of oxygen Nitrogen-treated males lived longer than air-irradiated males and competed successfully for females with untreated males Hooper[6] demonstrated, at the 98% level of male sterility in the Mediterranean fruit fly, *Certatis capitata*, that irradiation in nitrogen resulted in males which were three times more competitive than males irradiated in air

In order to bypass the debilitating effect of radiation and to produce competitive sterile males, we investigated the role of irradiation in nitrogen in induced sterility in *Aedes aegypti* Male pupae and 1-d-old adults were irradiated at 3,500, 7,000 and 10,000 r, respectively, either in air or in nitrogen and their competitive mating ability was tested against untreated males Nitrogen was allowed to flow through glass tubes containing pupae and 1-d-old males The chambers were clamped off and the "anaesthetized" condition of the mosquitoes was used as an indicator of the absence of oxygen The males were then allowed to acclimatize themselves to the nitrogen environment for 0.5 h before exposure to radiation Chambers containing males in a nitrogen environment and males in an air environment were exposed to gamma irradiation at the three doses Two days after exposure, experimental and untreated males were released simultaneously into colony cages containing 4-d-old virgin females The ratio of the mosquitoes in each cage was one treated male to one untreated male to one untreated female Each replicate contained fifty treated males, fifty untreated males and fifty untreated females Females were blood fed and egged separately The lack of hatchability or high egg hatch were used as indicators of whether a female was inseminated by a sterile or a normal male respectively

Table 1 gives the average hatchabilities of females inseminated by control and irradiated males and indicates that hatchability is a valid determination of whether an irradiated or control male inseminated a given female

Table 1 Average % Hatchability of Egg Papers after Irradiation of Inseminating Males

	Unirradiated (control)	3,500 rad	7,000 rad	10,000 rad
In air	96	30	0	0
In nitrogen	95	36	1.6	0

The data in Table 2 demonstrate that, in the conditions of this experiment, males irradiated to 7,000–10,000 r dose in the presence of nitrogen were as competitive as normal males in mating with females, whereas air-irradiated males were not Moreover, males exposed to a low dose of gamma radiation whether in air or nitrogen seemed to be three to four times as competitive as non-irradiated males These results indicate that nitrogen may protect males sterilized by irradiation sufficiently to permit the sterile male technique to be effective in the control of *Aedes aegypti* and other insect species

Table 2 % of Females Inseminated by Treated Males

Replicate No	Irradiation in air	Irradiation in nitrogen
Stage irradiated—male adults (3,500 r)		
	80 (20)*	70 (30)*
Stage irradiated—male pupae (7,000 r)		
1	26 (74)	55 (45)
2	12 (88)	51 (49)
3	18 (82)	46 (44)
Average	18 (82)	50 (50)
Stage irradiated—male adults (7,000 r)		
1	11 (89)	53 (47)
2	20 (80)	47 (53)
3	20 (80)	55 (45)
Average	17 (83)	51 6 (48 4)
Stage irradiated—male adults (10,000 r)		
1	24 (76)	55 (45)
2	13 (87)	52 (48)
3	18 (82)	51 (49)
Average	18 3 (81 7)	52 6 (47 4)

* Figures in parentheses indicate % females inseminated by untreated males

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New Complexes of Phenols and Lactams

COMPLEXES of drugs, including phenols, are of continuing interest, especially to pharmacologists, for purposes of solubilization, administration, antagonism, detoxification and controlled release[1-13] Schmulbach *et al*[14] studied the spectrography of phenols complexed with amides in solution but no products were isolated or characterized, only a 1 1 complex was suggested. Although polyvinylpyrrolidone (PVP) is known to form complexes with phenols[1-3,5,7], these have not been well defined because of molecular weight variation and steric inhibition of complete complexation

We have now found a number of phenols which form well defined, stable, crystalline complexes with several lactams Our N-substituted lactams (pyrrolidones) formed the complexes in the ratio of one amide to two phenolic hydroxyls The lactams unsubstituted on the nitrogen (2-pyrrolidone, ε-caprolactam) formed the complexes in the ratio of one lactam to one hydroxyl We were not able to isolate complexes involving phenols with substituents out of the plane of the ring such as *p*-nitro-, *p*-amino, *p*-phenylphenol or 1-hydroxy-anthraquinone Polymeric complexes from polyfunctional starting materials were not observed

The complexes were prepared by mixing the phenol with the lactam in the correct stoichiometric proportion, heating until liquid, then cooling (see legend to Table 1) Alterna-

Table 1 Summary of Complex Experimentation

Complex components					
A	*B*	*A B* (molar)	Reaction temp (°C)	Melting point, uncorrected (°C)	Recrystallization solvent
* HMBP	Phenol	1 4	50	54–56	Benzene
† HMBP	Hydroquinone	1 2	160	133–135	Water
‡ NMP	Hydroquinone	1 1	135	95–98	Toluene
		1 1	Boil	96–98 5	None
NMP	2,4,5-Trichlorophenol	1 1	90	62–64	Heptane
§ CHP	Hydroquinone	1 1	80	52–57	None
Pyrrolidone	Hydroquinone	2 1	130	135–138	Water
			130	130–132	Toluene
Pyrrolidone	Phenol	1 1	50	28–30	None
Caprolactam	Hydroquinone	2 1	130	117–119	Toluene
				117–119	Water
				116–119	None
Pyrrolidone	2,4,5-Trichlorophenol	1 1	90	73–77	Heptane
Caprolactam	Phenol	1 1	70	34–36	Heptane
HMBP	3,4-Dichlorophenol	1 4	85	54–57	Toluene
HMBP	2,4,5-Trichlorophenol	1 4	85	82–85	Heptane-toluene
HMBP	2,2′-Methylene-*bis*(4,6-dichlorophenol)	1 2	135	95–97	Heptane-toluene
HMBP	2.2′-Methylene-*bis*(3,4,6-trichlorophenol)	1 2	120	116–117	Cyclohexane-toluene

Most of the phenolics were regular stock items from chemical suppliers, better grades were used as received All the pyrrolidones were distilled These were prepared by well known methods[15] from ammonia or amines and γ-butyrolactone as in the following example A mixture of 604 g (5 2 mol) of hexamethylenediamine and 896 g (10 4 mol) of γ-butyrolactone was heated in an autoclave at 270° C for 7 h The product was distilled using a Vigreux column After stripping off the water of reaction, the N,N′-hexamethylene-*bis*-(2-pyrrolidone) (HMBP) distilled at 215° C at 0 2 mm Hg in 96% yield The HMBP was soluble in water, $n_D^{29}=1\ 5032$ (ref 16) Except as noted, the complexes were prepared without solvent, solvents were used at first to discover combining ratios Infrared curves showed that many bands of the starting materials persisted in the complexes but some were substantially shifted

* HMBP (1 mol) and phenol (4 mol) (thus one amide to two phenolic hydroxyls) were combined at 50° C Slight warming occurred immediately A hygroscopic crystalline mass formed on cooling Recrystallized from benzene, melting point, 54–56° C Calculated for $C_{38}H_{48}N_2O_6$ N, 4 46%, found 4 26%

† The complex was prepared neat, as tabulated, also by combining aqueous solutions It was prepared also by combining ammoniacal HMBP with aqueous hydroquinone For the recrystallized complex were calculated $C_{26}H_{36}N_2O_4$ C, 66 1%, H, 7 69%, N, 5 94% Found were C, 66 12%, 66 27%, H, 7 65%, 7 73%, N, 5 96% Infrared band shifts were observed

‡ NMP, N-methyl-2-pyrrolidone

§ CHP, N-cyclohexyl-2-pyrrolidone The product was chilled to 0° C to initiate crystallization

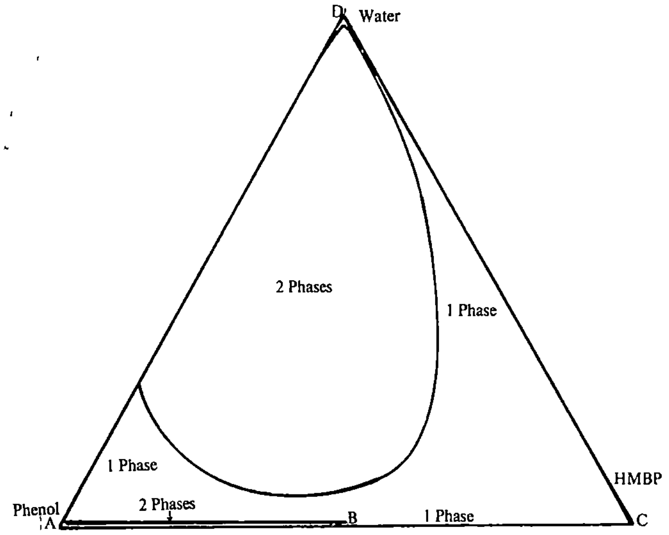

Fig 1 The water-phenol-hexamethylene-*bis*-(2-pyrrolidone) ternary system at 29° C The curved line was found by taking known solutions of two of the components in a stirred Erlenmeyer flask and, with the temperature at 29±0 5° C, titrating in the third component until the number of phases changed The line was approached from either side and the ends were derived from the literature[17] The line *AB*, displaced from the edge of the chart for visibility, was determined by titrating HMBP into phenol, any small second dimension being ignored

tively, the complex often precipitated from admixed solutions of the starting materials Crystallization was sometimes successful from water and usually successful from neutral organic solvents as benzene

The complexes were of constant composition regardless of starting composition and were crystals with sharp melting points The N,N′-hexamethylene-*bis*-(2 pyrrolidone) (HMBP) (melting point 26° C) complex with phenol (melting point 41° C) melted at 54–56° C The formation of the complex was exothermic Altered spectral (infrared) and physiological (germicidal) properties were observed

The complexes were thermally stable at least to their melting points They were stable in many organic solvents and many were stable in water The HMBP-hydroquinone complex was stable and could be formed in a series of liquids of various basicity, including aqueous ammonium hydroxide, pyridine, styrene, toluene, benzene, water, dioxane, acetic acid and monochloroacetic acid This complex could not be formed, and was decomposed in the presence of piperidine to give the piperidine salt of hydroquinone. Also it could not be formed and was decomposed by the presence of benzoquinone, the hydroquinone appearing as quinhydrone The HMBP-phenol complex was evidently stable in water because we observed a substantially reduced toxicity to *S aureus* The phase relationships in this ternary system are shown in Fig 1

The exact nature of the binding forces in the complex has not been elucidated On the basis of information now available we propose a plane-to-plane charge transfer stacking coupled with hydrogen bonding

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Chemosensory Mechanism in American Cockroach Olfaction and Gustation

ALTHOUGH numerous theories of olfaction and gustation[1–8] have been published, there is little experimental evidence on the energy-transfer mechanisms involved in the interactions of chemical messengers with proteinaceous receptors of sensory neurones One such mechanism, involved in the inhibition of feeding of *Periplaneta americana* and *Scolytus multistriatus* by various 1,4-naphthoquinones, has been extensively studied and partially interpreted behaviourally[9–16], ultrastructurally[10–16], electrophysiologically[10–16] and biochemically[10–16] These messenger naphthoquinones were shown to act through a selective reaction with sulphydryl[10–16] groups in a particular membrane-associated receptor macromolecule which was proven to be physically accessible *in situ*[17] to these chemicals through cuticular pores and tubules[10–16] in the walls of chemoreceptor sensillae on the insect's antennae This specific energy transfer resulted in disulphide-bond formation or thiol complexing[10–16], both of which are proven[18] mechanisms in certain proteins for causing conformational changes Such changes can alter the cationic permeability of macromolecules composing membranes[18] The messenger-altered cation permeability of the receptor thus can result in the generation of action potentials in the sensory neurone[10–16] Here we report certain physicochemical characteristics of the messenger-naphthoquinone receptor protein interactions as analysed in a deoxygenated system at physiological *p*H by the *in vitro* technique of dropping mercury electrode (DME) polarography (PO4 'Polariter', London Co) The polarogram is a current–voltage curve obtained by applying a gradually increasing voltage to a system and measuring the current flow at each potential Characteristic polarographic half-wave potential (that is, E 1/2) values for proteins were attributed exclusively to exposed, reactive sulphydryl, or reducible disulphide, groups[19–22] In our own investigations, the 'Triton' X-100-solubilized quinone-reactive receptor protein from the cockroach antennae gave a characteristic E 1/2 of −1,860 mV A control (non-quinone receptor) protein system composed of the saline-soluble proteins from the same antennae gave an E 1/2 of −1,800 mV Adding messenger 5-hydroxy-1,4-naphthoquinone (5×10^{-5} M) in the receptor preparation characteristically shifted the E 1/2 from −1,860 to −1,880 mV, another less repellent, or feeding-inhibitory, messenger, 2-methyl-1,4-naphthoquinone (5×10^{-5} M), only shifted the receptor E 1/2 to −1,875 mV Neither of these messenger quinones altered the −1,800 mV E 1/2 of the non-receptor control protein N-Ethyl maleimide (NEM), a highly specific thiol reagent, at 5×10^{-5} M in the receptor preparation shifted the E 1/2 from −1,860 to −1,890 mV In this −1,890 mV state, the receptor was non-reactive with messenger quinones Treatment of the receptor in the $-1{,}890$ mV state with the disulphide reducing agent, dithiothreitol (DTT), brought the E 1/2 of the receptor back down to $-1{,}860$ mV In this restored $-1{,}860$ mV state, the receptor again reacted with messenger quinones

The receptor protein was isolated from the antennae of adult male *P americana* using the techniques of Ferkovich and Norris[17] Two saline (0 9% NaCl), and then two 'Triton' X-100 in 0 9% NaCl, extracts were thus made from 100 pairs of antennae which had been excised proximally and immediately dropped into cold saline Protein concentrations were determined by the method of Lowry *et al*[23] using crystalline bovine serum albumin as a standard

In the polarographic analyses, the sample protein was diluted to 100 µg ml^{-1} of a potassium phosphate (0 1 M), *p*H 7 0, buffer which contained 25% (v/v) of 95% ethanol The polarographic sample was deoxygenated with nitrogen before and during the analysis Receptor samples (E 1/2= $-1{,}860$ mV) left exposed to atmospheric conditions on the laboratory bench for 24 h became non-reactive to quinone messengers, and then had E 1/2 values of $-1{,}890$ to $-1{,}900$ mV Ascorbic acid (0 01 M in the receptor-buffer preparation) maintained the receptor in its reactive (that is, $-1{,}860$ mV) state for up to 72 h

These results thus provide evidence that the energy-transfer mechanism for messenger quinone-receptor interactions in these chemosensory nerves involves characteristic shifts in the –SH/S–S– equilibrium in the receptor macromolecules Such a mechanism of predictable macromolecular reorientation in nerve membranes in response to specific messengers can bring about alterations of inorganic ion flows characteristic of nervous excitation and impulse conduction A natural system with variable sensitivities, such as now reported here, was postulated by Norris[24] as one basic mechanism for short- and long-term alterations of nerve membrane macromolecule state to binding functions[25] We believe learning and memory probably involve this fundamental mechanism

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Ranking Characters by a Dispersion Criterion

It is often proposed by taxonomists and ecologists that classifications and other related analyses should be based on the possible largest number of characters They believe that when large character sets are used the analysis will gain in accuracy, and the results will be more broadly applicable Yet sampling, computational and other logistic problems are often associated with the handling of large character sets Some characters may have to be deleted in the interest of more economical sampling and computations.

Appropriate criteria must be found to evaluate an individual character's relative importance I show that relative importance can be measured experimentally, based on a character's independent share of the total dispersion in a pilot sample of individuals, and the rank order of the importance values can be used to select those characters worth further investigation

I consider a pilot sample of N individuals described on the basis of p characters and with sample structure Q_{Np} I assume that the p characters represent a sub-sample of the total number of available characters P, the sample structure of which in the N individuals is Q_{NP}. I derive $\sigma(P,p)$ as a measure of the stress (or distortion) in Q_{Np} relative to Q_{NP} One may visualize Q_{Np} and Q_{NP} as $N \times N$ symmetric matrices which define the pairwise resemblance of the N individuals on the basis of their characters The elements may represent any kind of symmetric measures

When the goal is to reduce the number of characters, one may select them for deletion so that the stress function is minimized for any value of p, equivalently, the structure Q_{Np} will represent a best possible approximation to Q_{NP} The total number of distinct p samples that can be drawn from a P sample is $P!/(p!(P-p)!)$ One could proceed with the selection of the best p sample as follows Extract all distinct p samples, compute $\sigma(P,p)$ for each, and select the p sample for which $\sigma(P,p)$ is minimum For varying values of p, the results will provide a basis for the selection of those characters which should be considered further

There is one obvious defect in this procedure. the number of discrete p samples may be unmanageably large A computationally simpler method is needed Such a method may use the rank order of characters determined on the basis of a dispersion criterion given by the sum of squares (or some related measure). The steps include (1) Designate a data matrix by X, and its elements by X_{hj} The subscripts identify respectively a character (h) and an individual (j) There are P characters (row vectors) and N individuals (column vectors) (2) Centre the data within characters, as shown in equation (1), to obtain a new data matrix A with elements A_{hj} (In equation (1), $\bar{X}_h$ represents the arithmetic mean of observations for character h The data should be standardized if the characters used are not commensurable) (3) Compute a $P \times P$ dispersion matrix R for the characters on the basis of equation (2) (If the characters were standardized, R would represent a correlation matrix. An element of R is r_{hi} relating character h and character i.) (4) Compute the dispersion criterion S_1 (given by equation (3)) to identify character m the rank order of which is one (For computation of S_1, the value of subscript e is set at 1 Character m has maximum dispersion in the P sample) (5) Determine the character whose rank order is two, and rank all the remaining characters on the basis of criterion $S_2, \ldots , S_k, \ldots$ In each

Table 1 Sample Data

Characters		Individuals 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Mean $\bar{X}_h$
		Lengths (0 1 mm units)																	
Corolla	(X_1)	75	61	53	77	41	56	60	57	48	53	58	49	40	60	66	47	50	55 9
Calyx	(X_2)	27	17	20	19	16	18	19	28	29	35	37	29	30	36	45	36	41	28 4
Style	(X_3)	65	54	64	57	33	62	64	46	53	54	54	64	31	48	39	31	30	49 9
Corolla lobe	(X_4)	11	11	13	15	12	19	21	11	10	8	10	13	4	9	7	4	4	10 7
Pedicel*	(X_5)	15	16	13	12	11	14	21	17	16	14	18	26	6	13	16	10	7	14 4

* In 1 mm units

The entries in the table represent averages of ten independent measurements, 1–7 *Phyllodoce empetriformis* (Sm) D , 8–12 *Phyllodoce* × *intermedia* (Hook) Camp and 13–17 *Phyllodoce glanduliflora* (Hook) Coville The sample represents part of a larger collection presently under study in this department

case, the dispersion criterion is computed from a new residual R, in which the effect of those characters which were already ranked is removed from the correlations A residual element of R is defined by

$$r'_{hi} = r_{hi} - y_{hm} y_{im}$$

where r_{hi} represents an original value in R, or some residual portion of the original value, and y_{hm} and y_{im} are coordinates,

$$y_{hm} = r_{hm} / \sqrt{r_{mm}}$$
$$y_{im} = r_{im} / \sqrt{r_{mm}}$$

The subscript m identifies the character whose rank order has just been determined

$$A_{hj} = X_{hj} - \bar{X}_h \tag{1}$$

$$r_{hi} = \Sigma A_{hj} A_{ij}, j = 1, \quad , N \tag{2}$$

$$S_e = \max \left[\sum_{h=1}^{P} r_{h1}^2 / r_{11} \quad , \sum_{h=1}^{P} r_{hP}^2 / r_{PP}\right] \tag{3}$$

This ranking is based on each character's independent share (S_e) of the total dispersions given by the sum of the diagonal elements in R The best, or nearly the best, p sample is formed from the p highest ranking characters

S_e or $100 \, S_e / \sum_{h=1}^{P} r_{hh}$ may be used as a measure of sample weight, or "importance" value, for the characters But such a measure of importance will represent a meaningful input from a pilot study for further consideration in those analyses which are constrained because the r_{hi} represent meaningful spatial parameters in the sample space of the intended analysis, the intended analysis is performed on the same set of p characters, and the possibility exists to expand the character set to the same P characters from which the subset of p characters were originally drawn

When the r_{hi} are defined as sum of squares and cross products, the ranking by this method will represent valid input, for instance in sum of squares clustering[1], ordinations[2] which use Euclidean distance or vector scalar products, and methods which operate within the framework of an appropriate Euclidean sample space A quantity similar to S_e, but excluding self-comparisons, has been used[3] in classificatory analyses based on ranking.

The ranking method is illustrated in Table 1 The R matrix is defined as a correlation matrix (to remove the effect of scale differences of the characters from the analysis) given in Table 2 From these, I compute S_1=max (1 4429, 1 7641, 2 4983, 2 5301, 1 8457)=2 5301 corresponding to m=4 Rank 1 thus is assigned to character 4 This is the character which accounts for a maximum portion of the total dispersion in the 17 plant sample (Numerical results are given within computer rounding errors)

The first residual of R, after removing the effect of character 4 from correlations, is given in Table 3 The zero row and column are retained in this table to make it easier to keep track of those characters which are still remaining in the analysis From the first residual correlations I obtain S_2=max (0 9937, 0 7272, 0 7512, 0 0000, 0 9075)=0 9937 and m=1 This establishes 2 as the rank order for character 1

Similarly, S_3=max (0 0000, 0 5927, 0 5344, 0 0000, 0 8796)= 0 8796 and m=5, so the rank order for character 5 is 3, and S_4=max (0 0000, 0 3318, 0 2844, 0 0000, 0 0000)=0 3318, corresponding to m=2 The rank order for character 2 is 4, and 5 for character 3 In the last residual of R there is only one non-zero value (0 2648) located in the third diagonal cell

The results are summarized in Table 4 The total of the S_e values is 5, the same as the sum of the diagonal elements in the correlation matrix This implies that the ranking is based on truly orthogonal partitions

Table 2 Upper Half of the Correlation Matrix R for Five Characters Listed in Table 1

1 0000	−0 0622	0 5076	0 3467	0 2475
	1 0000	−0 4577	−0 7310	−0 1281
		1 0000	0 7546	0 6796
			1 0000	0 5533
				1 0000

Table 3 The First Residual of R Obtained by Removing the Effect of Character 4 from the Correlations Given in Table 2

0 8798	0 1913	0 2460	0 0000	0 0557
	0 4656	0 0940	0 0000	0 2764
		0 4306	0 0000	0 2621
			0 0000	0 0000
				0 6939

Table 4 Character Ranks and Other Ranking Statistics

Character in Table 1	Rank order (e)	Character's specific dispersion (S_e)	Relative importance ($100 \, S_e/\Sigma r_{hh}$)
X_1	2	0 9937	19 9
X_2	4	0 3318	6 6
X_3	5	0 2648	5 3
X_4	1	2 5301	50 6
X_5	3	0 8796	17 6
Totals		5 0000	100 0

The problem of identifying a cutoff point in the rank order, below which no character will be further investigated, will arise Ideally, the decision should be based on some statistical criterion which could facilitate a test for the hypothesis that the last k lowest ranking characters do not contribute significantly to dispersion in the sample Because I know of no such test, I suggest the use of an alternative method for determining the cutoff point: omit the last q characters whose importance value is zero or nearly so; compute the stress curve $\sigma(P,p)$ at fixed P and varying p representing samples of the first $P-q$, $P-q-1$, $P-q-2$, . highest ranking characters; inspect the stress curve and select a p sample in the region where the curve starts flattening off.

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Multivariate Analysis of the *Dryopithecus africanus* Forelimb

CORRECT interpretation of fossil postcranial remains is crucial to understanding primate phylogeny This is very apparent in the study of the postcranial remains of the East African Early Miocene hominoid *Dryopithecus africanus*[1] In 1951 Whitworth discovered a nearly complete forelimb from the Gumba Peninsula, Rusinga Island, Kenya, as part of an association with dental and cranial remains of *D africanus* The deposits date from 19 to 16 m y [2,3] Napier and Davies[3] concluded that the forelimb of *D africanus* showed many features reminiscent of monkeys, for example, colobines and atelines, which supposedly use their forelimbs alone for locomotion a significant amount of the time They further claimed that "in the absence of *a priori* evidence as to the probable nature of the fossil remains provided by the associated jaw fragments, it is to be doubted whether there would have been sufficient evidence from the forelimb bones alone to postulate the pongid affinities of *D africanus* " This view has gained wide acceptance[4–6]

Because many shared postcranial features of *Pan* and *Gorilla* were supposedly not present in *D africanus*, two alternative hypotheses concerning the *Pan–Gorilla* (and basal hominid) radiation were proposed (1) that the knuckle-walking adaptations of both *Pan* and *Gorilla* represent a case of extensive parallel postcranial evolution since the Early Miocene[7], or (2) that the *Pan–Gorilla* radiation must have occurred more recently than the Miocene[8–10]

Following Napier and Davis[3], it has been generally assumed that *D africanus* was postcranially most similar to the so-called "semi-brachiating" monkeys like *Presbytis* and *Colobus*[4,6] These two forms are active arboreal palmigrade quadrupeds Recent re-examinations of the forelimb anatomy of *D africanus* indicate that the view of *D africanus* as merely a "dental ape" might be in error. Many of the anatomical features of the *D africanus* forelimb most closely resemble *Pan*, and are markedly non-cercopithecoid-like (refs 10 and 11, and personal communication from A C Walker)

Deperet[13], in 1887, was the first to put forward the view, later often supported in the writings of Le Gros Clark[6], that postcranial bones of Tertiary apes resemble in various ways the same bones of living monkeys rather than those of hominoids the *scala naturae* Naturally, Miocene apes do share some structural features with monkeys that are not now seen in hominoids, but many of these primitive features are also found in lemurs and lorises, and thus can hardly be termed exclusively "monkey-like" For these and other reasons, the forelimb similarities of *D africanus* to cercopithecoid and ceboid monkeys seem to have been overemphasized.

Multivariate statistical analysis provides an effective way of establishing affinities between fossil and living primates[14,15] We have used the multivariate techniques of principal components and principal coordinates analysis, which do not necessitate previous categorization of specimens into groups[16,17].

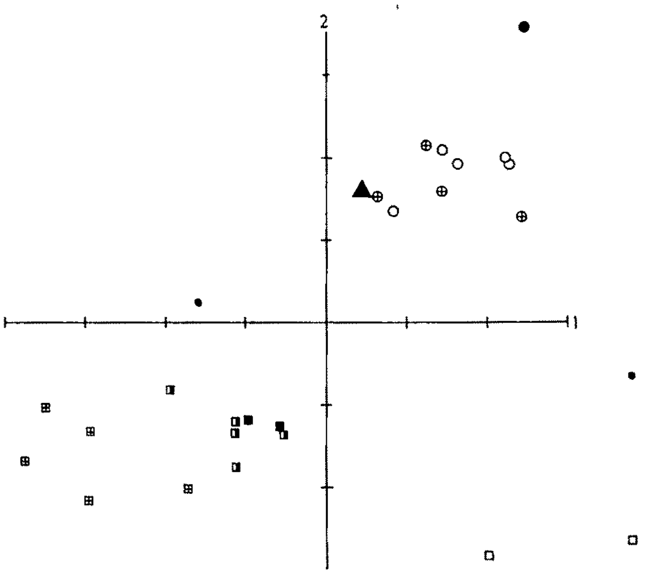

Fig. 1 Plot of the principal component scores of primate forelimbs along the first and second principal component axes, respectively subsuming 71 8 and 17 8% of the total variance ▲, *Dryopithecus africanus*, ⊕, *Pan paniscus*, ○, *Pan troglodytes*, ●, *Gorilla gorilla*, ■, *Presbytis* sp, ⊞, *Papio* sp, ◨, *Cercopithecus* sp, □, *Ateles* sp

To establish the locomotor affinities of *D africanus*, we performed components and coordinates analysis using sixteen indices of the forelimb listed originally by Napier and Davis[3] Indices rather than raw measurements were used in order to minimize the significance of size differences (see Table 1 for indices used) Twenty-five forelimb specimens were included in the sample one *D africanus*, four *Pan paniscus*, one *Gorilla gorilla*, five *Pan troglodytes*, two *Ateles*, two *Presbytis*, five *Papio* and five *Cercopithecus* All values are taken from Napier and Davis[3] except for *Gorilla* and *Pan paniscus*, which we measured. *Pan paniscus* indices were included because it is the pongid closest in size to *D africanus*, this reduces the disruptive effects of allometric differences

In Fig 1, there is a clear separation between pongids and monkeys, as well as a separation between the spider monkey and all other monkeys With respect to locomotion, the first component separates quadrupedal cercopithecoids from both knuckle-walkers (*Pan* and *Gorilla*) and the quadrupedal arm-swinger (so-called "semi-brachiator") *Ateles* The second component separates knuckle-walkers from all non-knuckle-walking quadrupeds With respect to both of these axes, the forelimb of *D africanus* falls among the apes, indicating that the total morphological pattern of the forelimb is pongid-like, not monkey-like The remaining axes fail to separate apes from monkeys, and thus are not particularly relevant for our purposes. These results were verified by a principal coordinates analysis on the same forelimb measurements (see Fig 2)

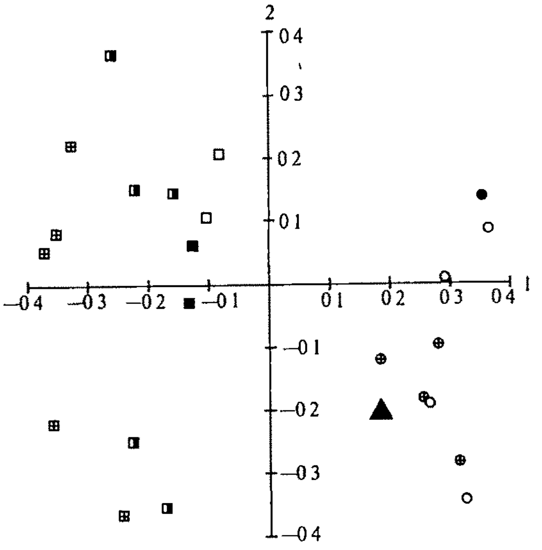

Fig. 2 Plot of the principal coordinate scores of primate forelimbs along the first two coordinate axes. Symbols as in Fig. 1.

The variates which contribute most to the separation seen in Fig. 1 can be determined by examining the weighting of each index in Table 1. The most important variates which affect the first two axes are indices 10, 8, 11, 9, 3 and 2. Because the heavy weightings of these indices are primarily responsible for both the separation between apes and monkeys and the placement of *D. africanus* among the pongids, the functional significance of these indices should be assessed.

Table 1 The Indices Used in the Principal Components Analysis and their Weightings for the First Three Components

Index	First component	Second component	Third component
(1) Groove	0.001	−0.050	−0.086
(2) Deltoid	0.103	0.168	−0.098
(3) Deltoid-latissimus dorsi	0.136	0.207	−0.210
(4) Supinator crest	−0.059	−0.004	−0.249
(5) Biepicondylar	0.017	0.117	0.038
(6) Articular width	0.001	0.076	−0.001
(7) Medial epicondyle	0.066	0.041	0.031
(8) Trochlear	0.195	0.786	0.465
(9) Brachial	−0.137	−0.224	0.047
(10) Radial neck	0.945	−0.282	0.012
(11) Ulnar styloid	−0.091	−0.385	0.798
(12) Relative metacarpal length	−0.004	0.053	0.040
(13) Relative phalangeal length	0.043	−0.059	−0.066
(14) Relative carpal length	−0.031	0.023	0.064
(15) Relative hand length	0.027	0.034	−0.073
(16) Relative humerus length	0.010	0.030	0.053
% of total variance	71.7	17.8	5.7

Indices are listed in order of appearance in Napier and Davis appendices I–IV, where they are defined[3].

The most significant index on the first axis, which separates knuckle-walkers and the arm-swinging *Ateles* from palmigrade quadrupeds, is the radial neck index. In forms such as *Ateles* which use their forelimbs alone for propulsion for a significant part of their daily activities, the radial neck is relatively long, as it is in *Limnopithecus*[18]. Such an anatomical arrangement augments the power of the biceps brachii muscle around the elbow joint by increasing the lever arm/load arm ratio of the radius. Powerful flexion and supination of the forearm are both necessary adaptations for animals which suspend and propel themselves by their forelimbs alone. In the pongids, who often climb by pulling themselves up with the forearms, the long radial neck is also important, although not as significant as in arm-swingers and brachiators (that is, gibbons).

Two other indices which are important contributors to separation along the first axis are concerned with the distal insertion of the deltoideus on the humerus. The low insertion of deltoideus characterizes pongids as opposed to cercopithecoids. This reflects the importance of the deltoideus in forms capable of powerful abduction of the forelimb.

On the second axis, the greatest discriminating index separating knuckle-walkers from all monkeys is the trochlear index. This index is also the second greatest contributor to the first component. A relatively high trochlear width in pongids is associated with high degrees of rotational ability in the forelimbs. In pongids, powerful forearm flexion is possible whether or not the hand is in the pronated or supinated position. The stability of the pongid elbow joint is maintained by the fit of the humerus and ulna (and by the ulnar collateral ligaments), regardless of the position of the radius. In monkeys, which are capable of only about 90° of supination, the proximal ulna is narrow (as is the corresponding trochlea of the humerus) and the radial head is oval in shape. Both of these bones are responsible for maintaining the integrity of the elbow joint in cercopithecoids[8]. Besides possessing a high trochlear index, *D. africanus* also has a rounded radial head.

The second most important index which contributes to the second axis of the principal components analysis is the ulnar styloid index, which is low in knuckle-walkers and high in monkeys and *D. africanus*. The length and morphology of the ulnar styloid process were considered by Napier and Davis[3] to indicate that *D. africanus* had a monkey-like wrist joint. Lewis[12,19], however, has analysed the wrist joints of monkeys, apes and *D. africanus* and has stressed that several pongid features do appear in the *D. africanus* wrist joint. Lewis has suggested that this is an adaptation facilitating suspensory posture, however, these features of wrist morphology are more reminiscent of knuckle-walkers, especially *Pan*, than of brachiators, that is, gibbons.

The brachial index is also important in discriminating knuckle-walkers from monkeys along both axes in Fig. 1. The low brachial index in *D. africanus* suggests that it was not adapted for either fast digitigrade running or habitual arm-swinging.

It can be concluded that the forelimb of *D. africanus* is much more similar to pongids than to monkeys with respect to the sixteen indices devised by Napier and Davis[3]. The similarity of these indices in fossil and modern apes goes far to dispel the widely held assumption that Miocene apes only resemble modern apes in their dental anatomy. Whether or not *D. africanus* was a knuckle-walker is a question requiring further investigation, but from this analysis it can at least be seen that *D. africanus* was not a *Presbytis*-like quadruped, as has been suggested. Considering rates of evolution and the fact of mosaic evolution, an early Miocene possible ancestor of *Pan* should not be expected to have been identical to the modern chimpanzee postcranially. The strong implication is, however, that if *D. africanus* was not a knuckle-walker, it may have been in some ways preadapted to that form of locomotion. A possible model could be the hand posture of certain New World monkeys when walking on the ground. Weight is borne on the heel of the hand and the dorsum of the phalanges, which are "tucked under" (personal communication from M. Schon). There is no need to consider the modern postcranial and locomotor similarities of *Pan* and *Gorilla* as a puzzling case of parallelism. Instead, by Miocene times at least one species of fossil ape had developed a postcranial anatomy foreshadowing that of *Pan* and *Gorilla* , this ape thus represents an ideal structural ancestor, not only dentally but also postcranially, for one or more of the modern knuckle-walking apes

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Positive Allometry of Antlers in the "Irish Elk", *Megaloceros giganteus*

Megaloceros giganteus, the famous Eurasian giant deer of Late Pleistocene times, possessed the largest antlers ever known reliable estimates of their total span range up to 4 m

An allometric hypothesis has long been maintained[1] to circumvent the earlier conclusion[2] that a non-Darwinian orthogenesis had sealed the fate of *Megaloceros* under the oppressive weight of its own enlarging antlers Simpson[3], for example, has argued that selection for an advantageous increase in body size entailed relatively larger antlers as a correlated response—producing a phenotype which, as a whole, proved superior to smaller bodies with relatively smaller antlers Though this interpretation has the status of textbook dogma[4,5], it is based on no biometrical data whatever

The allometric hypothesis requires two very different tests (1) Did *Megaloceros,* at its maximal body size for deer of the subfamily Cervinae, lie on a line fitted for adults of all cervine deer? (2) Was the age-standardized variability among adult stags of *Megaloceros* so arranged that selection for larger body sizes entailed relatively larger antlers? Interspecific and intraspecific allometry are quite distinct phenomena[6,7]

(1) Data for maximal antler length plotted against shoulder height for living cervines and *Megaloceros* show strong positive allometry[8] in a reduced major axis fit for error in both variates

$$\text{Antler length}=0.0342\ (\text{shoulder height})^{1.85}$$

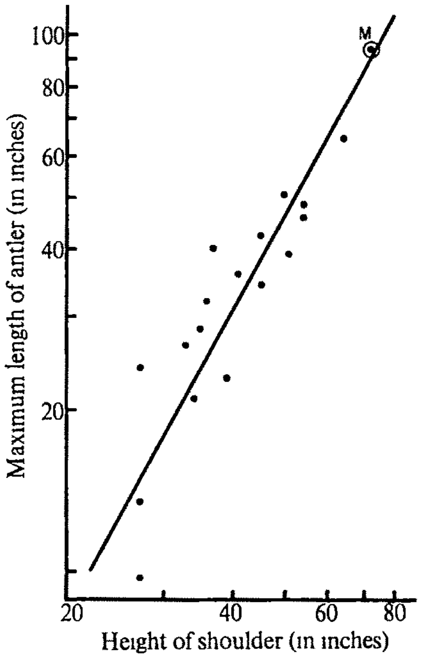

Fig. 1 Allometry among adult cervine stags, each point represents a single species *Megaloceros* is the circled point at maximum size

As shown in Fig 1, *Megaloceros* lies right on the curve and, therefore, represents an expected antler size for deer of its body size True elk (including the American moose) have relatively small antlers for their body size , giant deer display the expected antler dimensions (Moose, as members of the subfamily Alcinae, are not included in Fig 1 The relatively small antlers of moose compared with those of giant deer may reflect the contrasting habitats of dense thicket and open ground)

(2) To test the more important second hypothesis, I measured seventy-nine skulls and attached antlers of *Megaloceros* from museums and homes in Eire, Great Britain, continental Europe and the United States All specimens were found in Ireland or the Isle of Man In Ireland, *Megaloceros* is known only from sediments of the Allerod interstadial, a brief period lasting only 1,000 yr[9–11] (G F Mitchell (personal communication) doubts the assignment of Savage[11] and asserts that no postglacial *Megaloceros* have been found in Ireland) Thus, potential geographical and phyletic components of variation are reduced to a practical minimum for vertebrate palaeontology , one is dealing primarily with true intra-populational variation For antler size, I used a compounded measure of antler length, antler width and lengths of the brow and second tine (the three characters were weighted equally (combining the two tines as a single character) by equalizing the means, applying correlations to each value, summing for each specimen and dividing by three) Because complete skeletons are uncommon, I used basal length of the skull (ventral lip of foramen magnum to anterior tip of premaxillaries) for my measure of body size This measure has several desirable features (i) it rapidly reaches a final adult size and remains constant throughout life[12,13] , (ii) it has a very strong relationship to body length with slight positive allometry[14] (this positive allometry is a welcome feature for a conservative hypothesis, if antlers are positively allometric to the skull, then they will increase with even stronger positive allometry to total body length) , (iii) it is the standard dimension of body size in most allometric literature on vertebrates[6,7] Fig 2 shows a grouped plot (at 10 mm intervals of skull length for adult stags), positive allometry is very strong and the log correlation coefficient is 0.987.

$$\text{Antler size}=0.0000437\ (\text{basal length})^{2.584}$$

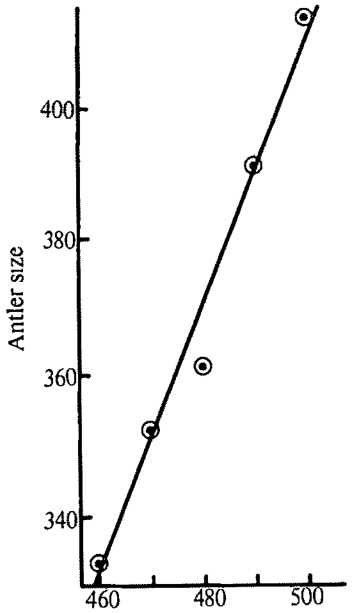

Fig 2 Intraspecific allometry among adult stags of *Megaloceros* Data are grouped at 10 mm intervals of skull length, scales are logarithmic

(The log correlation coefficient for raw data is a highly significant 0 568 An attempt to remove the effect of age upon the antlers by correcting according to the most reliable criterion of pedicel height yielded no significant difference either in the correlation or the parameters of the regression) The bony pedicel from which the antlers spring decreases in height with the addition of each new pair of antlers[15,16] (By plotting the parabolic relationships of antler size against pedicel height (both young and old stags have smaller antlers than animals in their prime), a criterion for the removal of age effects can be constructed)

The allometric relation is a fact, but the standard interpretation—that the enormous antlers are a passive consequence of advantageously larger bodies—need not be maintained The relation caters just as well to the idea that selection operated on the antlers or on both antlers and body Traditionally, the antlers have posed a dilemma because all authors upheld the (often hidden) assumption that they must function as weapons for battle against predators or rival males (they are poorly designed and over massive for such a role) Field studies of cervids and bovids[17–20] have, however, shown that antlers often function primarily as "visual dominance-rank symbols"[21] As devices for display rather than combat, relatively larger antlers would have an immediate and potent adaptive significance they would have assured access to females and success in reproduction Moreover, the antlers of *Megaloceros* are ideally formed for such a role Deer with palmated antlers show the full palm in prominent display[22] To do this, fallow deer and caribou must rotate their heads from side to side (personal communication from V Geist, December 1972) If *Megaloceros* had to swing its 85 pound antlers about its 5 pound skull, the resultant torque would have posed a mechanical problem But, uniquely among deer with palmated antlers, *Megaloceros* displayed its full palm when it simply looked straight ahead (Fig 3) (Once the display hypothesis is entertained, this point is so obvious that it was noted independently by at least three observers R Coope, V Geist and myself, priority must go to Coope)

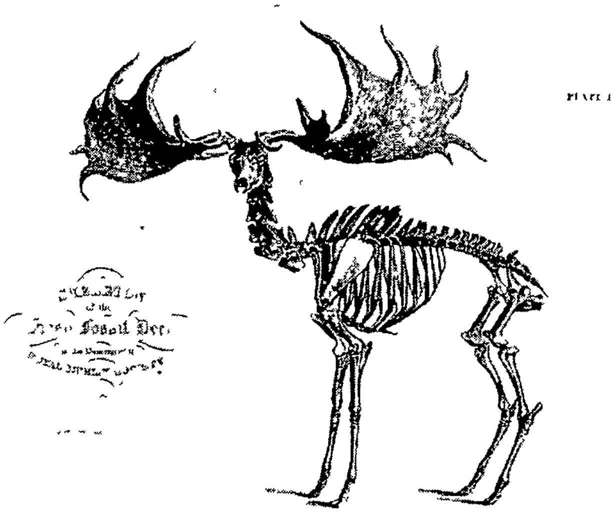

Fig. 3 *Megaloceros* showing the full palm display when looking directly forward This figure, published in 1830 (ref 23), represents the second complete (and first reasonably accurate) mounted skeleton It is still displayed at the National Museum of Ireland in Dublin

I conclude that *Megaloceros* exploited the positive allometry of its antlers to attain the selective advantages of both larger bodies and relatively larger antlers

Stephen Jay Gould

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Reference Abbreviations

From September 1 it is *Nature's* intention that all abbreviations of references should conform to the style of the *World List of Scientific Periodicals,* fourth ed (Butterworth, 1963–65) The changeover will be gradual and authors submitting manuscripts from now on are asked to ensure that the references are written appropriately

Obituary

T. G. B. Osborn

THEODORE GEORGE BENTLEY OSBORN, Professor Emeritus of Oxford and Adelaide Universities, was born on October 2, 1887 He was educated at Burnley Grammar School and the University of Manchester His early research was on the fungi and was done mainly during the period 1908–1912, when he was Lecturer in Economic Botany in the University of Manchester In 1912 he was invited to become Professor of Botany in the University of Adelaide and Consulting Botanist to the Government of South Australia Shortly before going to Australia, he had married Edith May Kershaw, who was also a botanist and associated with the work of the Botany Department in Adelaide They had three sons, Peter, Andrew and Richard, all of whom served in World War II, Andrew, an RAF pilot, was killed in action

When he established the Department of Botany at Adelaide in 1912 Osborn was only twenty-five years old and youthful in appearance He was fond of the story of how he went into the examination hall, which was being supervised by a middle-aged woman who had not met him, and asked for the Botany I paper She brought him the paper, and when he said, "And while I'm here I'll have a look at the Agricultural Botany paper, too," she replied, "You'll do nothing of the sort, you'll just sit down there and get on with your Botany I"

Osborn recognized the need for establishing plant ecology in Australia, and began the work on the ecology of South Australia for which he was well known He occasionally undertook other work such as the descriptions of the morphology of *Isoetes* and *Phylloglossum* In collaboration with Professor R S Adamson (University of Capetown) he published on the ecology of the Ooldea district in 1922 and on the ecology of the Mount Lofty Ranges in 1924 One of his most important contributions was the establishment, in 1924, of the Koonamore Vegetation Reserve, which is now the oldest biological station in Australia with continuous records The first and important work on grazing of natural vegetation in arid regions resulted from the collaborative work of Osborn, Wood and Paltridge in this area

In 1928, Osborn became Professor of Botany at the University of Sydney and he set about reorganizing the undergraduate courses there He himself took the first year lectures and plant physiology, as well as ecology At first he continued to clear up his research arising from the work in arid zones but increasingly he became interested in the vegetation of coastal New South Wales In 1930 he gave the Livingstone Lectures entitled *Plant Life in the Sydney District*, with an ecological approach He was interested in the xerophytic properties of the plants characteristic of this relatively high rainfall area In 1932 his Presidential Address to the Linnean Society of New South Wales was on *The Plant in Relation to Water*, with special reference to the properties of xerophytes Later Osborn's interest in ecology was associated with starting others on ecological descriptions of parts of New South Wales In that period he published a paper jointly with Robertson on the ecology of the Myall Lakes vegetation

Osborn became Sherardian Professor of Botany and a Fellow of Magdalen College, Oxford, in 1937 The Oxford Department was very poorly housed in cramped surroundings in an old building in the Oxford Botanic Garden The Botanic Garden at Oxford, founded in 1621, had become somewhat neglected but Osborn stimulated collaborative work with the garden, and this continued strongly even after the department, due to Osborn's initiative, moved to the new laboratories As *Nature* said at the time, "the great improvements in the gardens, which have occurred in recent years, owe much to his expert supervision and advice" The achievement of causing a new laboratory to be built was an important contribution, particularly in the difficult period for planning and constructing buildings in the war and immediate post war years At the same time Osborn spent much time on university business, and was in demand for advisory work for the Agricultural Research Council, of which he was a member (1945–49), and other public bodies

In 1953 Osborn retired from the Chair at Oxford and returned to Australia After a short period of residence in Melbourne he returned to Adelaide to live and became Deputy Master of St Mark's College, of which he had been one of the founders He gave some courses in the Adelaide Botany Department and regularly attended the departmental seminars Many younger members of staff and students appreciated conversation with this veteran of three different universities, he had the distinction of being Professor Emeritus of both Oxford and Adelaide Universities In 1960 Osborn married Marjorie Sabine and they both contributed to the social life of the Adelaide Botany Department

Osborn was a good lecturer and teacher who succeeded in attracting students of quality, they valued the association with a man who attempted to give them an understanding of high standards of science Former Australian students include J G Wood (formerly Professor of Botany, Adelaide), N A Burges (Vice-Chancellor, University of Northern Ireland), M R Jacobs (formerly Director General of Forestry), D Martin (Officer in Charge, Tasmanian Regional Laboratory, CSIRO), H K C Mair (Director and Chief Botanist, National Herbarium, Sydney), Sir Rutherford Robertson (Head, Research School of Biological Sciences, Australian National University), Lilian Fraser (Chief Biologist, Division of Science Services, NSW Department of Agriculture), Joyce Vickery (formerly Botanist, NSW Department of Agriculture), N C W Beadle (Professor of Botany, University of New England) and Gwenda Davis (Associate Professor of Botany, University of New England)

Announcements

International Meetings

August 27–September 1, **Eighth Leucocyte Culture Conference.** (Professor Kerstin Lindahl-Kiessling, University of Uppsala, The Institute for Medical Genetics, V Agatan 24, S-75220 Uppsala, Sweden)

August 31–September 1, **The European Symposium of the International Association of Forensic Toxicologists.** (Faculty of Pharmaceutical Sciences, Dept of Toxicology, State University of Gent, Hospitaalstraat 13, 9000 Gent, Belgium)

September 2–7, **First International Congress for Bacteriology.** (Secretariat, 'Kenses', P O Box 16271, Tel Aviv, Israel)

September 2–7, **International Association of Microbiological Societies.** (The International Congress for Bacteriology, P O. Box 16271, Tel Aviv, Israel)

September 2–7, **First International Congress on Mercury.** (Primer Congreso Internacional del Mercurio, Instituto Tecnologico Metalurgico 'Emilio Jimeno', Facultad de Ciencias, Universidad de Barcelona, Barcelona 14, Spain)

September 2–8, **International Union of Food Science and Technology.** (Mr G D Brown, The Bord Rank Research Centre, Lincoln Road, High Wycombe, Bucks)

September 3–6, **International Symposium on Liquid Scintillation Counting.** (Mr M A Crook, The Society for Analytical Chemistry, 9–10 Savile Row, London W1X 1AF)

September 3–6, **Second International Symposium on Nuclear Quadrupole Resonance Spectroscopy.** (Dr Arturo Colligiani, NQR Symposium, Laboratorio di Chimica Quantistica, Via Risorgimento 35, I-56100 Pisa, Italy)

September 3–7, **Third International Conference on Molecular Sieves.** (Professor W M Meier, Institut fur Kristallographie der ETH, Sonneggstrasse 5, 8006 Zurich, Switzerland)

September 3–7, **Isotopes and Radiation Techniques in Studies of Soil Physics and Drainage in Relation to Crop Production** (Mr Y Barrada of the Joint FAO/IAEA Division of Atomic Energy in Food and Agriculture, International Atomic Energy Agency, PO Box 590, Karntnerring 11, A-1011 Vienna, Austria)

September 3–7, **Third International Conference on Chemical Thermodynamics and a Symposium on Physicochemical Techniques at High Temperatures.** (Professor F Kohler, Institute of Physical Chemistry, University of Vienna, Wahringer Strasse 42, A-1011 Vienna, Austria (Conference); Professor C B Alcock, Dept of Metallurgy and Materials Science, University of Toronto, Toronto 5, Canada (Symposium)

September 4–6, **The Phytochemical Society.** (Dr J G Vaughan, Biology Dept , Queen Elizabeth College, Campden Hill Road, London W8, or Professor C F Van Sumere, Laboratorium voor Plantenbiochemie, Rijksuniversiteit Gent, 35 K L Ledeganckstraat, 9000 Gent, Belgium)

September 5, **Particle Size Analysis in the Sub-Micrometre Range.** (The Society for Analytical Chemistry, Analytical Division, Chemical Society, 9–10 Savile Row, London Q1X 1AF)

September 5–7, **International Symposium on the Biology of the Male Gamete.** (The Executive Secretary, Linnean Society, Burlington House, Piccadilly, London W1)

September 5–7, **Nuclear Structure · Heavy Ions and Related Topics.** (Nuclear Physics Sub-Committee, Institute of Physics, 47 Belgrave Square, London SW1X 8QX)

September 5–7, **Magnetic Bubbles.** (Dr E A D White, Electrical Engineering Dept , Imperial College, Exhibition Road, London SW7)

September 5–12, **Second International Congress of Plant Pathology.** (Dr Roy D Wilcoxson, The American Phytopathological Society, 1821 University Ave , St Paul, Minnesota 55104, USA)

September 5–15, **Large Scale Applications of Superconductivity and Magnetism.** (Drs Simon Foner and Brian B Schwartz, Francis Bitter, National Magnet Lab , Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA)

September 7–9, **More Learning—Less Teaching.** (Meeting Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX)

September 7–11, **Economic and Social Values in the Assessment of Crop Protection and Pest Control Methods.** (Mr D T. Saggers, Chesterford Park Research Station, Saffron Walden, Essex)

September 8–14, **First International Congress of Ecology.** (International Congress of Ecology, c/o Royal Netherlands Academy of Sciences and Letters, Kloveniersburgwal 29, Amsterdam, The Netherlands)

September 8–15, **Eighth International Congress of Chemotherapy.** (Scientific Secretary, Dr Polyxeni Kntomichalou, PO Box 1554, Athens, Greece)

September 9–14, **Third International Congress of the International Radiation Protection Association.** (Mr John C Villforth, Secretary, Bureau of Radiological Health, FDA, 5600 Fishers Lane, Rockville, Maryland 20852, USA)

September 10–11, **Third Biennial Symposium on Turbulence in Liquids.** (Dr J L Zakin, Dept of Chemical Engineering, University of Missouri-Rolla, Rolla, Missouri 65401, USA)

September 10–11, **Solid State Devices Conference.** (The Solid State Physics Sub-Committee of the Institute of Physics, 47 Belgrave Square, London SW1X 8QX)

September 10–12, **Carbonization and Graphitization.** (Conference Secretary, Dr H Marsh, Northern Coke Research Labs , School of Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU)

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Applications are invited for the following posts in the Faculty of Agriculture

SENIOR LECTURER/LECTURER IN AGRICULTURAL BOTANY Candidates should have a good honours degree in Botany, Agricultural Botany or Agriculture plus a higher degree and/or research experience in Botany or Agricultural Botany Appointee will be required to teach Agricultural Botany including ecology and agrometeorology to undergraduate students He will also be expected to carry out research in his field of speciality and supervise postgraduate students

SENIOR LECTURER/LECTURER IN SOIL SCIENCE Applicants must possess a higher degree, preferably a Ph D in any field of Soil Science He should have considerable experience in University teaching and research

LECTURER/ASSISTANT LECTURER IN PEDOLOGY Candidates should have a good basic degree in Agriculture and at least a Masters degree or postgraduate Diploma in Pedology Teaching and research experience in the field of Pedology would be an advantage Appointee will teach the course in Soil Science/Pedology and be expected to initiate and supervise research in this field

Salary scales Senior Lecturer T£2 380 to T£2 800 per annum, Lecturer T£1 898 to T£2 318 per annum, Assistant Lecturer T£1 260 to T£1,915 per annum (T1=£1 10 sterling) The British Government may supplement salary in range £550 to £950 per annum (sterling) for married appointee or £300 to £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages This supplementation is unlikely to be applied to appointment at Assistant Lecturer level F S S U Family passages, biennial overseas leave

Detailed applications (2 copies), including curriculum vitae and naming 3 referees, should be sent by air mail not later than September 4 1973 to the Chief Academic Officer University of Dar es Salaam, P O Box 35091, Dar es Salaam, Tanzania Applicants resident in U K should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road London W1P 0DT Further particulars may be obtained from either address (151)

UNIVERSITY OF DAR ES SALAAM
TANZANIA

Applications are invited for the following posts in Department of Geography

SENIOR LECTURER/LECTURER IN HYDROMETEOROLOGY OR HYDROLOGY Candidates should have expertise in the fields of Hydrometeorology or Hydrology

ASSOCIATE PROFESSOR/SENIOR LECTURER IN HYDROLOGY Candidates should have expertise in the fields of surface Hydrology and/or Water Management Experience of Administration the design of courses in Hydrology and of teaching is essential Experience in the tropics or developing areas will be advantageous Appointee will be responsible for the organization and co-ordination of degree courses in Hydrology based essentially on the standard WMO syllabus, but with modifications to suit local Tanzanian conditions The course is organized within the Faculty of Science through the co-operation of the Departments of Physics, Chemistry Mathematics and Geography Appointee will be expected to build up the training course to cater for the expanding needs of Government for graduates with experience in Hydrology and Water Resources

Salary scales Associate Professor T£2,800 to T£3,220 per annum, Senior Lecturer T£2 380 to T£2 800 per annum, Lecturer T£1,898 to T£2,318 per annum (T£1=£1 10 sterling) The British Government may supplement salaries in range £550 to £1,100 per annum (sterling) for married appointees or £300 to £850 per annum (sterling) for single appointees (normally free of all tax) and provide children's education allowances and holiday visit passages F S S U Family passages biennial overseas leave

Detailed applications (2 copies), including curriculum vitae and naming 3 referees should be forwarded by air mail not later than September 4, 1973, to the Chief Academic Officer, University of Dar es Salaam P O Box 35091, Dar es Salaam Tanzania Applicants resident in U K should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT Further particulars may be obtained from either address (152)

UNIVERSITY OF GLASGOW
DEPARTMENT OF BOTANY
POST-DOCTORAL RESEARCH ASSOCIATE

A post-doctoral research associate is required to assist Dr A Crozier with an SRC supported investigation into gibberellin metabolism in *Phaseolus coccineus* seedlings The appointment is for three years beginning October 1, 1973, and the initial salary is £1,764 per annum (under review) plus F S S U

Applications with the names of two referees, should be sent not later than September 8, 1973 to Professor M B Wilkins, Department of Botany, The University of Glasgow, Glasgow G12 8QQ, and in reply please quote Ref No 3332M (145)

THE WORLD HEALTH ORGANIZATION

invites applications for the following posts
at its Headquarters in Geneva

1. TWO SCIENTIST/MEDICAL OFFICERS

A. To assume responsibility for managing one or more Task Forces and for accelerating the development of new fertility regulating agents.

Ph D in biomedical sciences OR a medical degree with postgraduate training in biomedical sciences in addition to several years' experience in biomedical research management

Salary ranges from US$ 16,555 to US$ 20,130 (net of tax) per annum.

B. To be responsible for the Research Training component.

Medical degree or a Ph D in biological or related sciences. Experience in research administration and in the organisation of training courses highly desirable Research experience in the field of fertility regulation.

Salary ranges from US$ 13,578 to US$ 17,568 (net of tax) per annum.

2. SOCIAL SCIENTIST/MEDICAL OFFICER

To assume major responsibility for the planning and management of a Task Force on the Acceptability of Fertility Regulating Methods

Graduation from a university with a doctorate degree in Anthropology Sociology, Psychology, Social Psychology and Demography, OR graduation from a medical school with specialization in epidemiology or social medicine

Salary ranges from US$ 13,578 to US$ 17,568 (net of tax) per annum.

3. TECHNICAL OFFICER

To assist in the administration and implementation of the Clinical Research Centre component

University degree (preferably at Master's level or equivalent) in a relevant biomedical discipline (pharmacy, biology or chemistry). Additional training in Business Administration or related subjects an advantage Practical experience in clinical trial administration.

Salary ranges from US$ 11,283 to US$ 15,093 (net of tax) per annum.

EMPLOYMENT CONDITIONS:

Initial two-year contract Additional benefits include cost of living and dependants' allowances, children's education grant, health scheme and pension fund Home leave travel every other year.

Applicants should write quoting the reference "HR Vacancies" attaching a summary curriculum vitae with detailed work experience. Those having the requisite preparation and experience may be requested to complete a WHO Personal History Form. Candidates under active consideration will receive a reply.

Chief, Personnel,
World Health Organisation,
Avenue Appia,
Geneva, Switzerland

(148)

HOECHST PHARMACEUTICALS RESEARCH LTD.

Diagnostics Research

The laboratories of the new Hoechst Research Centre at Milton Keynes, Bucks, will become operational at the end of this year We are now seeking senior staff for the Diagnostics Research Department to work in the field of diagnostic immunoassay methods, for which class facilities will be provided. Scientists with experience and demonstrated research ability in the following areas are required

Radioimmunoassay. Applicants should have several years' experience in the development of radioimmunoassay methods, including the preparation and testing of reagents

Steroid Chemistry. Applicants should have several years' experience in steroid chemistry A knowledge of radio-labelled steroid sythesis would be desirable

Protein Chemistry. Applicants should be familiar with modern methods of isolation, purification and analysis of mammalian proteins and hormones

Immunology. Applicants should be familiar with animal immunisation methods and the purification and detailed characterisation of antisera

Attractive salaries will be offered The Company also operates a merit bonus scheme and free membership for employees and dependants of the PPP Health Scheme. The pension scheme is contributory Assistance with house removal is also available

Would candidates in the first instance please write with fullest possible details to

Personnel Officer, Pharmaceuticals Division,
Hoechst UK Limited, Hoechst House, Salisbury
Road, Hounslow, Middlesex, Tel 01–570 7712
Ext 3082

(136)

Toxicologist

Dog & Primate studies c£4,000

Our client, Inveresk Research International, is a major independent British Research Institute Its function is to provide the most modern facilities, equipment and expert scientific staff to carry out research and development under contract for industry, government agencies and international bodies

The Institute is just embarking upon a considerable growth and expansion programme, in connection with which we currently seek an experienced toxicologist to take direct charge of acute and chronic toxicity studies in dogs, marmosets and baboons (total colony size well in excess of 1 000 animals)

Much importance is attached to researching and developing new model systems and techniques, and considerable recent attention has been directed to such areas as fertility studies in the baboon and investigation of the behaviour of socially organised primate groups as sensitive test systems for evaluation of anti-anxiety and anti-depressant drugs

Candidates should be life science graduates aged 28–42 with experience of toxicological dosing of dogs and monkeys In addition, they must have a keen interest in developing the science of toxicology, and enjoy meeting people outside their immediate environment to discuss scientific and toxicological problems of mutual interest

The successful candidate will be accorded wide authority and responsibility in running his team and he will be based at the Elphinstone Research Centre, located in pleasant countryside near the university city of Edinburgh

Salary is negotiable within wide limits around £4000 Benefits and conditions of service are good and include free life assurance and BUPA membership, and four weeks holiday per year Extensive financial assistance will be given towards removal and re-establishment costs

Please write briefly and in complete confidence for an application form, or ring if you would like to discuss the position further

A E F Chandler, M A, Ph D, D I C,
Talentmark Limited, King House,
5/11 Westbourne Grove, London W2 4UA
Tel 01-229 2266

Talentmark
Biomedical and Scientific Consultants

(217)

THE QUEEN'S UNIVERSITY OF BELFAST

Temporary Lectureship in Department of Applied Mathematics and Theoretical Physics

This post is tenable for one year from October 1, 1973 Preference will be given to candidates with interests in one or more of the following fields Scattering Theory, Upper Atmospheric Physics, Astrophysics, Operational Research, Statistics The salary, according to qualifications and experience, will be in the range £1,929 to £2,388 per annum Applications should be received by September 1, 1973

Further particulars may be obtained from the Senior Assistant Secretary (Personnel), The Queen's University of Belfast, Belfast BT7 1NN, Northern Ireland (Please quote Ref 73/N)

(166)

BIOCHEMIST OR PHYSICAL BIOCHEMIST

required to work on mechanisms controlling energy metabolism in muscle, with particular reference to ATPase activity Published work of merit would be expected, in fields such as regulation of ion transport, calcium ion flux in relation to activation of muscle, or multiple metabolic pathways and their switching mechanisms Qualifications Applicants should have a First or upper Second Class honours degree, together with appropriate postgraduate research experience Salary For a suitably qualified candidate the appointment is expected to be at Senior Scientific Officer level, salary scale £2,615 per annum to £3,640 or higher for a particularly well-qualified applicant Superannuation under F S S U with a 4½ per cent allowance of gross salary to offset contributions Application forms Secretary, Meat Research Institute, Langford, Bristol BS18 7DY

(179)

NEW ZEALAND

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH

Applications are invited for the undermentioned vacancy

SCIENTIST, AGROMETEOROLOGY SECTION,

CROP RESEARCH DIVISION,

LINCOLN, NEAR CHRISTCHURCH

Salary Up to $NZ8,749 per annum depending on qualifications and experience

Duties To work on the energy balance of crop production under the climatic conditions of Central Canterbury and to investigate crop and soil response to agricultural management practices

Qualifications desired A degree in environmental physics or related subject, experience in crop experimentation and knowledge of instrumentation an advantage

Passages Fares for appointee and if married, his wife and family will be paid

Incidental expenses Up to £55 for a single man and £183 for a married man can be claimed to cover the cost of taking personal effects to New Zealand

Application forms and general information are available from the High Commissioner for New Zealand, New Zealand House, Haymarket, London SW1Y 4TQ, with whom applications will close on **September 14, 1973.**

Please quote reference B13/18/124 when enquiring

(139)

UNIVERSITY OF NEW ENGLAND

ARMIDALE, NEW SOUTH WALES

LECTURER IN PHYSICAL AND INORGANIC CHEMISTRY

Applicants should hold a higher degree, preferably with specialization in inorganic/analytical chemistry, and with either teaching or research experience Duties will comprise teaching in physical and inorganic chemistry at first-year level and advanced teaching in inorganic and analytical chemistry

It is hoped that the successful applicant will be able to commence duties about February 1, 1974

Salary $A8,698 to $A11,982

Conditions include provision for travel and removal expenses In addition, superannuation is available, together with assistance in buying or building a home and study leave Study leave grants are available and credit may be granted for existing study leave entitlement

Further information may be obtained from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572)

Applications close on **September 28, 1973.**

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Metropolitan Police
Forensic Science Laboratory

Microbiologist

■ Set up and operate Microbiology Section for identification of bacteria, fungi and yeasts in casework samples ■ Conduct research on application of microbiology to forensic problems.

☐ Degree/HNC in Microbiology/Bacteriology ☐ Research experience desirable ☐ Post-qualification practical experience essential ☐ Age under 32 ☐ Appointment as Scientific Officer (£1493-£2352), Higher Scientific Officer (£2251-£2842) or Senior Scientific Officer (£2790-£3815) according to age, qualifications and experience ☐ Ref. SA/1/DR ☐ Closing date 31 August 1973.

☐ Application forms from the Secretary, Room 733, New Scotland Yard, Broadway, London SW1H 0BG, telephone 01-230 3122 (24 hour answering service).

Ministry of Agriculture, Fisheries and Food
Royal Botanic Gardens, Kew

Taxonomist/Botanist

■ Conduct taxonomic research in Herbarium ■ Identify living and preserved plants ■ Reorganise and curate collections ■ Answer enquiries on taxonomic work.

☐ 1st or 2nd honours degree in Botany ☐ At least 2 years' postgraduate experience ☐ Age under 30 ☐ Appointment as Higher Scientific Officer (£2166-£2757) ☐ Ref SB/1/AH ☐ Closing date 31 August 1973

☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service)

British Museum (Natural History)
Department of Entomology

Entomologists

■ Investigate proposed specifications for establishing identity, purity and potency of medicinal chemicals ■ Devise methods of analysis ■ Report to technical committees ■ Laboratory will be moving to Canons Park, Edgware.

☐ Degree, HNC or equivalent in Chemistry or Pharmacy ☐ Practical experience in quality control an advantage ☐ Age under 30 ☐ Appointment as Higher Scientific Officer (£2251-£2842) or Scientific Officer (£1493-£2352) ☐ Ref SB/1/KD ☐ Closing date 7 September 1973.

☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service)

Science group
CIVIL SERVICE

(174)

UNIVERSITY OF LEICESTER

BOTANICAL LABORATORIES

RESEARCH TECHNICIANS

RESEARCH TECHNICIAN Grade 3 (salary scale £1,539 to £1,794) Appropriate ONC or OND or higher qualification To assist in the continuous culture of higher plant cells and in studies of their metabolism

JUNIOR TECHNICIAN (research) whose work will involve the culture of plant cells and training in electron microscopy Candidates should have appropriate science subjects in GCE and be between 17 and 19 years of age (salary in the range £789 to £933 per annum)

Both appointments to date from September 1 or October 1, 1973 Letters of application quoting 2 referees to be addressed to Professor H E Street, Botanical Laboratories, University of Leicester, Leicester LE1 7RH

(138)

UNIVERSITY OF BATH

SCHOOL OF BIOLOGICAL SCIENCES

TECHNICIAN

The successful applicant for the above position will be concerned with the preparation of cytological material for transmission electron microscopy He or she should have experience in fixation, embedding, and ultra microtomy, and should be qualified to O N C level or equivalent

The appointment will be for approximately three years in the first instance, supported by an S R C grant

Starting salary £1,539 per annum

Application forms and further particulars are available from The Registrar (S), University of Bath, Claverton Down, Bath BA2 7AY, and should be returned as soon as possible quoting reference 73/100

(158)

HOECHST PHARMACEUTICALS RESEARCH LTD.

Head of Administration

Hoechst, one of the largest chemical companies in the world, is building a new Pharmaceutical Research Centre at Milton Keynes in Buckinghamshire which will become operational in early 1974 The Research Director would now welcome applications for the senior post of Head of Administration to work closely with him to create and then manage an administration system for the laboratories

The successful applicant will enjoy the challenge of establishing an administrative system in a new research organisation with a high proportion of graduate staff He will establish procedures necessary for proper finance and research monitoring and planning, and will liaise in this area with other Hoechst Groups in the U K and Germany In addition to the members of his own team, he will supervise the work of the Laboratory Manager and Technical Information Officer.

Qualifications Applicants should have administrative experience at a policy-making level in an organisation with a high proportion of graduate scientific staff

Knowledge of the German Language and of systems analysis would be valuable

An attractive salary will be offered The company also operates a merit bonus scheme, and free membership for employees and dependents of the PPP health scheme The pension scheme is contributory Assistance with house removal is also available

Would applicants in the first instance write, with fullest possible details, to

Personnel Officer, Pharmaceutical Division,
Hoechst U K Limited, Hoechst House,
Salisbury Road, Hounslow, Middlesex TW4 6JH
Tel 01-570 7712, Ext 3082

(253)

HOECHST

Nutritional Biochemist

A vacancy exists in a multi-disciplinary research team studying dietary and therapeutic factors involved in the control of human obesity Candidates should be graduates in biochemistry or nutrition, preferably with a strong interest or practical experience in this or closely related fields

Beecham Research Laboratories are part of the Beecham Group and this appointment will be taken up at the research station at Walton Oaks, Tadworth which is situated in a pleasant area of Surrey, within easy reach of London

A good starting salary will be offered and reviewed regularly There are generous fringe benefits including sick pay, non-contributory pension and a U K bonus scheme

Please reply briefly, stating age, qualifications, and experience to

Personnel Officer,
Beecham Research Laboratories,
Nutritional Research Centre,
Walton Oaks, Tadworth, Surrey.

BRL

(159) 1972

QUEEN MARY COLLEGE
UNIVERSITY OF LONDON

DEPARTMENT OF ZOOLOGY AND COMPARATIVE PHYSIOLOGY

Applications are invited for a Lectureship from October 1, 1973, or as soon thereafter as possible Preference will be given to candidates with interests in Ecological or Physiological aspects of fresh water biology

Salary scale £1,923 to £4,548 per annum, plus £162 London Allowance F S S U membership. Application forms and further details from The Registrar (N), Queen Mary College, Mile End Road, London E1 4NS, to be returned by August 22 (251)

SIR WILLIAM DUNN SCHOOL OF PATHOLOGY
UNIVERSITY OF OXFORD

CYTOGENETICIST.

Required to take part in investigations on malignancy under the direction of Professor Henry Harris Experience with chromosome banding techniques highly desirable The appointment will be for a period of three years in the first instance Salary according to qualifications and experience on the appropriate University scale

Apply to Professor Henry Harris, Sir William Dunn School of Pathology, University of Oxford

(222)

READVERTISEMENT

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)

APPOINTMENT OF PHYSICIST

A Physicist is required to study interactions between the constituents of milk and cream, subsequent to homogenization, that affect the long-term stability of the product The person appointed would be expected to contribute to the solution of kindred problems encountered in the selective ultrafiltration and concentration of milk and milk products by cold processes

Applicants should have a 1st or Upper 2nd honours degree in physics or in biophysics, or an equivalent qualification Evidence of interest, or preferably postgraduate training, in colloid science, membrane transport, or the physics of macromolecules, would be sought

Appointment would be in the grade of Scientific Officer (£1,318 to £2,177) or Higher Scientific Officer (£2 076 to £2,667), depending on age, qualifications and experience Application forms are obtainable from the Secretary, N I R D , Shinfield, Reading RG2 9AT Quote Reference 73/7

Previous applicants should not re-apply (12)

UNIVERSITY OF NEWCASTLE UPON TYNE
DEPARTMENT OF GEOLOGY

RESEARCH OFFICER

A vacancy exists for a Research Officer in the above department who would work under the direction of Professor T S Westoll, F R S , on Vertebrate Palaeontology with special emphasis on lower vertebrates

The position is expected to be tenable for 3 years from October 1, 1973, subject to the Conditions of Service laid down by the University It is particularly suitable for a recent graduate in Geology with good Zoological background, or in Zoology with some Geological background A successful candidate may register for a higher degree, and though preference will be given to recent graduates other qualified persons are not excluded

The salary scale, at present subject to review, is Junior Research Officer £1,236 by £78 to £1,392 by £84 to £1,476, Research Officer £1,764 by £159 to £1,923 by £156 to £2,079, with F S S U

Applications (three copies), giving a full curriculum vitae and the names and addresses of three referees, should be made to the Registrar, The University, 6 Kensington Terrace, Newcastle upon Tyne NE1 7RU, not later than August 25, 1973 (162)

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG, SOUTH AFRICA

and the South African Institute for Medical Research

SECOND CHAIR OF PATHOLOGY (ANATOMICAL) IN THE SCHOOL OF PATHOLOGY

Applications are invited for appointment to the above-mentioned post on the joint staff of the University and the Institute in the School of Pathology Duties are to be assumed as soon as possible

The salary attached to the post is R12,000 per annum In addition a pensionable allowance of 15 per cent per annum is payable on the above salary, which will soon be consolidated in the salary Benefits include an annual bonus, pension and medical aid facilities and a housing subsidy, if eligible

Intending applicants should obtain the information sheet relating to this post from the Registrar, University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, or from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

Applications should be lodged not later than **August 31, 1973.** (185)

LISTER INSTITUTE OF PREVENTIVE MEDICINE

CARDIOTHORACIC INSTITUTE, THE BROMPTON HOSPITAL

Applications are invited for a three-year appointment to work on the separation and characterization of the macromolecular constituents of bronchial mucous secretion The project, which is supported by the MRC, will be under the joint direction of Professor L Reid (C-T I) and Dr J M Creeth (L I P M), the appointee will be located initially at the Lister Institute Applicants should have a Ph D or equivalent Experience in the fields of proteins or glycoproteins, and familiarity with ultracentrifuge methods, would be an advantage Salary up to £2,062 (by £108 to £2,278) plus £162 London allowance plus F S S U , depending on experience For full details of the position, apply to Dr J M Creeth, Department of Biophysics the Lister Institute of Preventive Medicine, London SW1W 8RH (154)

QUEEN MARY COLLEGE

University of London

SCHOOL OF BIOLOGICAL SCIENCES

Applications are invited for a LECTURER and a TEMPORARY LECTURER in the Department of Plant Biology and Microbiology Preference will be given to candidates with interests in Developmental or Population Genetics, and Mycology, but recruitment will not necessarily be restricted to these fields The appointment will date from October 1, 1973, or as soon as possible thereafter Salary scale £1,929 to £4,548 per annum plus £162 London Allowance

Application forms and further particulars from the Registrar (N), Queen Mary College, Mile End Road, London E1 4NS, to be returned by September 3 (184)

UNIVERSITY OF WESTERN AUSTRALIA

PERTH

Applications are invited for the following appointment

> LECTURER, SENIOR LECTURER or ASSOCIATE PROFESSOR in the Department of Zoology Enquiries are invited from persons actively working and teaching in marine biology The Professors (Professor H Waring and Professor A R Main) would be interested in submissions from people engaged in any of the numerous facets of marine work including physiology, quantitative studies and/or fisheries biology, and will be pleased to supply detailed information The level of appointment will depend upon qualifications and experience The appointee will be expected to take a considerable part in undergraduate teaching of general invertebrates in all years of the B Sc pass and honours courses, and to supervise Ph D students in this specialist field

The salary ranges are Associate Professor—$A15,940 per annum , Senior Lecturer—$A12,268 to $A14,308 per annum , Lecturer—$A8,698 to $A11,982 per annum Benefits include superannuation similar to F S S U , fares to Perth for appointee and dependent family, removal allowance, study leave and long service leave and housing loan scheme Further information may be obtained from the Staffing Officer, in the University

Applications in duplicate stating full personal particulars, qualifications and experience, should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, by **September 8, 1973.** Candidates should request three referees to write immediately to the Staffing Officer

Further particulars, conditions of appointment and application procedure are available from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572) (183)

ROSS POULTRY LTD

SENIOR RESEARCH GENETICIST

The breeding sector of this major international company is responsible for the design and implementation of the breeding programmes for egg layers, broilers, turkeys and pigs From a breeding Department Head Office in Scotland, elite, grandparent and parent stocks are distributed world wide to forty-five countries There are currently nine overseas breeding programmes implemented and controlled by the company

Due to the tragic and untimely death of Dr R Osborne, M A , Ph D , F R S E , Dip An Gen , the vacancy has arisen for an experienced geneticist to head the company's research team Although qualifications are important, experience with some of the livestock mentioned would be invaluable The successful applicant will have an aptitude for the statistical aspects of quantitative genetics, and will also be able to demonstrate, by experience in the field of animal breeding, an ability on breeding programme design and thinking within a range of wide parameters

A company car, contributory pension fund and competitive salary which is negotiable and will be based on experience, is offered

Applications including a full curriculum vitae to be sent in complete confidence to

The Chairman and Managing Director,
Ross Poultry Ltd ,
Imperial House, 61 – 65 Rose Lane,
Norwich NOR 12B, Norfolk

(246)

Lister Institute of Preventive Medicine, Elstree, Herts.

vacancy for

Medically Qualified Virologist

Applications are invited for the post of Deputy to the Head of the Research and Development Unit at the Elstree Laboratories of the Lister Institute of Preventive Medicine Applicants must be medically qualified and have some research experience in virology and immunology

The duties include the supervision of the assay of viral vaccines, the routine inoculation of the Institute staff and basic research related to viral vaccines. Salary, according to age and experience, will be similar to University scales including F S S U contributions

Applications, with names and addresses of three referees, to the Secretary, The Lister Institute of Preventive Medicine, Elstree, Herts.

(208)

Opportunity Overseas

This appointment is wholly financed by the British Government under Britain's programme of aid to the developing countries

British Solomon Islands

AGRICULTURAL MARKETING SPECIALIST

Required to be concerned with the preparation and marketing of local and overseas crops and the establishment of copra produce buying points Applicants, who should normally be citizens of and permanently resident in the UK, should be experienced in marketing and the preparation of tropical crops for market Appointment for 2 years

SALARY, subject to UK income tax, £4,000 pa plus a variable tax free overseas allowance in range of £570–1375 pa

Other benefits include free family passages, paid leave, children's education allowances and free accommodation and medical attention

For full details, application form and booklet about the British Solomon Islands, please apply giving age and brief details of qualifications and experience to

Appointments Officer,
Foreign and Commonwealth Office,

Overseas Development
Administration

Room E301, Eland House,
Stag Place, London SW1E 5DH

(176)

MONASH UNIVERSITY

Melbourne, Australia

DEPARTMENT OF GENETICS

SENIOR TEACHING FELLOW

Applicants should normally have completed a M Sc or Ph D degree and will be responsible for the preparation and presentation of practical classes in Genetics in various years of the science course The successful applicant will be expected to start as early in 1974 as possible Facilities will be available for the successful applicant to undertake research in collaboration with the staff members of the Department

Salary range $A7,270 to $A8,698 per annum

Benefits Travelling expenses for appointee and family, removal allowance, temporary housing for an initial period, repatriation

Further general information and details of application procedure are available from Mr J D Butchart Academic Registrar, Monash University, Wellington Road, Clayton, Victoria 3168, Australia, or from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572) Enquiries may be addressed to Professor B W Holloway, Chairman of the Department in the University, from whom a detailed statement of current departmental research interests is available

Closing date **September 7, 1973**

The University reserves the right to make no appointment or to appoint by invitation

(203)

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

(UNIVERSITY OF READING)

VACANCY IN THE FEEDING AND METABOLISM DEPARTMENT

A research scientist is required to investigate the flow of intestinal digesta in dairy cattle The immediate responsibility is to continue the development of apparatus for measurement and sampling of digesta passing through the duodenum an apparatus is at the prototype stage There will be a continuing responsibility for supervision of the application of the technique in important collaborative studies involving a number of other workers In parallel to these duties the successful candidate will be encouraged to develop his own line of work into an aspect of gastrointestinal funotion revelant to the programme of the department

Applicants should have a 1st or upper 2nd class honours degree in physiology, biochemistry, or veterinary or agricultural science and postgraduate experience involving duodenal cannulae or other aspects of gut function

Appointment would be in the grade of Higher Scientific Officer (£2,076 to £2 667) or Senior Scientific Officer (£2,615 to £3,640), depending on qualifications and experience A non-pensionable allowance of 4½% of basic salary will be paid to offset contributions under F S S U arrangements Application forms are obtainable from the Secretary, NIRD, Shinfield, Reading RG2 9AT Quote reference 73/24 (41)

THE QUEEN'S UNIVERSITY OF BELFAST

DEPARTMENT OF ELECTRICAL AND ELECTRONIC ENGINEERING

Applications are invited for a LECTURESHIP in the field of Control Engineering in the Department of Electrical and Electronic Engineering tenable from October 1, 1973, or such other date as may be arranged The person appointed will be expected to take an active part in the lecturing and laboratory activities relevant to his subject He will also be expected to undertake research in his field of interest Currently there is a strong interest in the application of control to batch production systems and any interest in this field will fit in well with Departmental research objectives Salary scale is £1,929 to £4,548 with contributory pension rights under the F S S U Initial placing on the scale will depend on experience and qualifications

Further particulars may be obtained from the Senior Assistant Secretary (Personnel), The Queen's University of Belfast, Belfast BT7 1NN, Northern Ireland (Please quote Ref 73/N)

(168)

IMPERIAL COLLEGE

Department of Chemistry

Applications invited for S R C Post-doctoral Research Assistantship on Interaction of Osmium Tetroxide with Model and actual Biological Tissue and Membrane Materials Tenable for one year in the first instance with possible extension to second year salary up to £1,929 plus £162 London allowance with F S S U, commencing preferably on October 15, 1973 Previous experience in preparative organic or organometallic chemistry or biochemistry is desirable Applications (with curriculum vitae and names of two referees) to Dr W P Griffith, Chemistry Department, Imperial College, London SW7 2AY

(193)

IMPERIAL COLLEGE

Department of Chemistry

Applications invited for a Post-doctoral Research Assistantship to investigate the Structure and Reactivity of an interesting new type of Organo-Metallic complex Experience in either organic or inorganic chemistry desirable Salary will be up to £2,058 plus £162 London allowance, depending on age and experience, with F S S U Appointment renewable with the usual salary increments

Applications, in writing, giving full details with two referees, to Dr B C Challis, Chemistry Department, Imperial College, London SW7 2AY (192)

CENTRAL PUBLIC HEALTH LABORATORY

Colindale Avenue, London NW9 5HT

TECHNICIAN

(H N C or A I M L T in medical laboratory sciences) required for a large centralized media production department This post involves supervisory duties and offers opportunities to use technical and organizational abilities Salary according to qualifications and experience

Written applications giving age, full details of qualifications and experience, together with names and addresses of two referees, to the Personnel Officer at the above address (197)

UNIVERSITY OF SHEFFIELD

DEPARTMENT OF HUMAN BIOLOGY AND ANATOMY

LECTURER required, preferably with special interests in Human Biology, Anthropology or related fields Candidates should be capable of teaching topographical anatomy to medical and dental students

Applications should be sent to the Registrar and Secretary, The University, Sheffield S10 2TN, by August 21 1973 Further details may be obtained by writing informally to Professor R Barer Quote Ref R 53/G (10)

Respiratory Physiologist looking for challenge and involvement

The Huntingdon Research Centre is the recognised international leader in contract research in the life sciences area Rapid and sustained growth has taken place, and we now wish to recruit an additional Respiratory Physiologist to work in this demanding and challenging environment.

We are looking for a male graduate, who possesses a degree in one or more of the following subjects Physiology, Zoology or Biology. An additional advantage would be experience in the use of radio-isotopes and the handling of laboratory primates and rodents – although this is not essential. The successful applicant will join a team working, in modern and fully-equipped laboratories, on respiratory physiology as it relates to inhalation toxicology, with particular reference to the effects of tobacco smoking.

The Centre is located near Huntingdon in an attractive part of the country, with easy access to London by road and rail We offer excellent working conditions together with progressive general benefits, a highly competitive salary and the usual pension and other fringe benefits.

Please write or telephone for an application form to John Halliday, Personnel Officer, Huntingdon Research Centre, Huntingdon PE18 6ES, (Telephone Woolley 431), quoting Reference No. 257.

H.R.C.

Huntingdon Research Centre

(250)

TRENT POLYTECHNIC, NOTTINGHAM

DEPARTMENT OF LIFE SCIENCES

PRINCIPAL LECTURER IN PHYSIOLOGY/PHARMACOLOGY

To lead the existing team of Physiologists with respects to present coursés and those being developed in Paramedical studies, Nursing and Environmental Health

LECTURER GRADE II IN MICROBIAL GENETICS

A Biochemist, Microbiologist or Geneticist is required with expertise in Microbial Genetics

Salary scales Principal Lecturer, £3,581 by £102 (4) to £3,989 (Bar) by £102 (5) to £4,499, Lecturer Grade II, £2,515 to £3,243

Further details and form of application may be obtained from The Chief Administrative Officer, Trent Polytechnic, Burton Street, Nottingham NG1 4BU A self-addressed foolscap envelope should be enclosed with the enquiry Closing date August 24, 1973

(142)

UNIVERSITY OF NEWCASTLE UPON TYNE

DEPARTMENT OF PHYSICAL CHEMISTRY

ELECTRON MICROSCOPIST

Applications are invited for a Postdoctoral Research Associate to study structures of cokes, carbons and graphites by electron microscopy The Associateship, sponsored by the S R C, will normally be tenable for three years

Salary scale £1,929 to £2,058 to £2,223 per annum over three years with F S S U (Scale under review)

Applications, accompanied by a curriculum vitae and the names of two referees, should be forwarded, as soon as possible, to Dr H Marsh Northern Coke Research Laboratory,' Department of Physical Chemistry, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU (164)

North Manchester Regional Virus Laboratory

VIROLOGY

(Principal Biochemist Grade)

(Salary Scale: £3516–£4599)

This new post is in a small but rapidly expanding routine diagnostic virology unit situated at Booth Hall Children's Hospital, 5 miles north of Manchester City Centre The Scientific Officer will be responsible – under the Consultant Virologist – for the overall management of the North Manchester Regional Virus Laboratory which comprises of a team of 8 Research is actively encouraged

The successful applicant will have a research degree in Virology and service laboratory experience The laboratory may be visited by prior arrangement with the Consultant Virologist, Dr Maurice Longson (Tel 061-740 2254)

Application forms (to be returned before August 20) and further details are available from **Mrs. F. Moody, Personnel Officer, Booth Hall Hospital, Charlestown Road, Manchester M9 2AA. (Quote Ref. 17089.)**

(223)

THE ASSESSMENTS DEPARTMENT
of the
NATIONAL RADIOLOGICAL PROTECTION BOARD
requires
SCIENTISTS

interested in the evaluation of hazards to man from ionizing radiation and the measurement techniques used for making these assessments The Department undertakes experimental and theoretical studies of a wide range of sources of radiation exposure of the general public and to occupational groups These studies include the public health implications of radioactivity released to the environment and of novel industrial and commercial uses of radioactive material and ionizing radiation The evaluation of instrumentation used in radiological protection is a significant part of the work of the Department The Department provides advisory services to Government Departments, public bodies and industry

Candidates will normally be expected to have a good degree in physics or another appropriate subject Experience relevant to some aspect of radiological protection would be an advantage but recent graduates will be considered Appointment will be in the grade of Scientific Officer or Higher Scientific Officer depending on the level of qualification but exceptionally well qualified and experienced applicants may be considered for appointment as Senior Scientific Officers

The posts are mainly at Harwell but some successful applicants may spend the first year of their service at the Board's premises at Sutton, Surrey

The salary scales appropriate to these appointments are

Scientific Officer	£1,415–£2,330 per annum
Higher Scientific Officer	£2,225–£2,855 per annum
Senior Scientific Officer	£2,800–£3,895 per annum

For further information and an application form write or telephone to

Personnel Officer (Ref. A.35),
N.R.P.B., Harwell, Didcot, Berks
Tel. No. Rowstock 600 (STD Code 023-583) Ext. 33.

Closing date for receipt of application forms, Friday, August 31

(190)

ASSISTANT PLANT BREEDER WANTED

To take charge of Amenity Grass Breeding programme and Evaluation of Cereal Varieties at an advanced breeding stage

Qualifications required a good knowledge of grass breeding methods, if possible in amenity grasses, ability to design and lay out trials and analyse the results obtained Knowledge of cereal variety evaluation would be an advantage, but not essential

It should be appreciated that the breeding work involved is specifically aimed at the production of new varieties rather than fundamental research into plant breeding problems

Applications should be made to Managing Director Sinclair McGill Limited, P O Box 23, 67 Kyle Street, Ayr KA7 1RY, from whom further information is available if required (43)

DEPARTMENT OF MICROBIOLOGY
GUY'S HOSPITAL MEDICAL SCHOOL
RESEARCH ASSISTANT

required for one year in the first instance in a team studying Viral Transformation in Relation to Membrane Changes and Regulation of Cell Growth Some postdoctoral experience in virology or membrane biology desirable Salary up to £2,388 according to experience, plus London allowance and superannuation

Applications, with curriculum vitae and names of two referees, should reach the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, by August 31 (64)

UNIVERSITY OF DUNDEE
DEPARTMENT OF ANATOMY
TUTOR IN HISTOLOGY

Applications are invited from suitably qualified science or medical graduates for a tutor to assist in the teaching of histology to medical dental and science students The successful candidate will have the opportunity of playing a part in the design of new teaching techniques He or she will also be encouraged to undertake research, preferably in a field involving electron microscopy or histochemistry The post is tenable for twelve months beginning on October 1, 1973 The salary will be in the region of £1,600

Applications quoting Ref EST/58/73J, and including a curriculum vitae, a list of publications, if any, and the names of two referees, should be sent to the Secretary, The University, Dundee DD1 4HN, by August 30 (143)

IMPERIAL COLLEGE
Department of Chemistry

Applications are invited for a Post-doctoral Research Assistantship (S R C) to study n m r Spectra of Complexes of High Coordination Number in collaboration with Dr D F Evans

Appointment for two years at initial salary of £1,929 plus £162 London allowance with F S S U Applications with names of two referees should be sent to Dr D F Evans, Chemistry Department, Imperial College, London SW7 2AY (191)

THE BRITISH COUNCIL
SRI LANKA (CEYLON) COMMONWEALTH EDUCATION COOPERATION

THE UNIVERSITY OF CEYLON, COLOMBO, requires from December 1973 a SENIOR LECTURER/LECTURER IN PHYSICS to consolidate the introduction of new experiments at all levels of undergraduate teaching Candidates should have a postgraduate degree from a university in Britain and relevant research and experience 73 PU 94A

THE UNIVERSITY OF CEYLON, PERADENIYA, requires a SENIOR LECTURER/LECTURER IN SOIL MICROBIOLOGY by December/January 1973/74 Candidates should possess a Ph D in soil microbiology from a university in Britain and have relevant teaching experience Experience in research would be an advantage 73 OU 43A

Salary £3,691 to £4,907 per annum according to experience Married overseas allowances within the following ranges accompanied £494 to £156, unaccompanied £379 to £41 The usual allowances and benefits will be granted including accommodation travel and children's allowances Two-year contract Candidates should be citizens of and normally resident in the U K

Write quoting relevant reference number to the British Council (Appointments), 29 Bressenden Place, London SW1E 5DD, for further particulars and application form to be completed as soon as possible

(232)

MEAT RESEARCH INSTITUTE
VETERINARY RESEARCH OFFICER/SENIOR VETERINARY RESEARCH OFFICER

Applications are invited for a new post in the Abattoir Section which will be concerned initially with investigations into stress and disease transmission during transport and lairing of slaughter stock in relation to carcass quality Applicants should have a veterinary degree, preferably with an intercalated qualification in physiology

SALARY V R O £2,445 to £3,095 per annum or S V R O £3,095 to £3,742 per annum according to postgraduate experience Superannuation under F S S U, with a compensatory non-pensionable allowance of 4½ per cent of basic salary

Application forms Secretary, Meat Research Institute, Langford, Bristol BS18 7DY (Quote ref AC18)

Applicants from the Agricultural Research Service should submit their applications through their present Directors if they wish to be considered for the award of "public interest" transfer terms

(200)

Im Zuge des weiteren Ausbasues unseres Biochemica Forschungszentrums in Tutzing am Starnberger See in der Nahe von Munchen suchen wir einen jungeren

Mikrobiologen oder Biotechnologen

der uber Erfahrungen auf dem Gembiet der Zuechtung von Biomasse verschiedenster Mikroorganismen verfügt

Fur diese interessante und sehr vielseitige Stelle suchen wir einen praxisorientierten Bewerber, der nach Moglichkeit Industrie-erfahrung besitzen sollte Gute Kenntnisse der Biochemie und der biochemischen Analytik werden ihm die Einarbeitung erleichtern

Wenn Sie diese Aufgabe interessiert, bitten wir um Ihre Bewerbung mit Lebenslauf, Lichtbild und Unterlagen uber Ihren bisherigen beruflichen Werdegang Wir antworten rasch

mannheim boehringer
diagnostika
therapeutika

Boehringer Mannheim GmbH—Bereich Personal 6800
Mannheim 31—Sandhofer Strasse 116—Deutschland

(205)

ST MARY'S HOSPITAL MEDICAL SCHOOL

(UNIVERSITY OF LONDON)
Paddington, London W2 1PG

POSTDOCTORAL RESEARCH FELLOW

Applications are invited from postdoctoral graduates with experience in human or animal metabolic research to join a team in Paediatric Unit The post will require the supervision of 2 projects concerned with (1) The bioavailability of certain heavy metal compounds of environmental significance (2) The development and application of new stable isotope techniques for the study of mineral metabolism in the human infant

Tenure of the post limited to 2 years from date of appointment Salary according to age, qualifications and experience on scale to maximum of £4,500 per annum Further particulars from Dr D Barltrop (Tel 01-723 1252 Ext 110) Applications to The Secretary (Ref PN) (172)

AGRICULTURAL RESEARCH COUNCIL

POST-DOCTORAL RESEARCH CHEMIST

A Post-doctoral Research Chemist is required for a project concerned with establishing mechanisms of degradation of organophosphorus insecticides in soil and vegetation The work will be carried out at the Chemical Defence Establishment, Porton Down, Salisbury, Wiltshire

Applicants should have some experience in modern spectroscopic, chromatographic and other analytical techniques and have some background in organic chemistry

The appointment, which will be for two years, will be as Higher Scientific Officer (£2,076 to £2,667 per annum) or Senior Scientific Officer (£2,615 to £3,640 per annum), the grade and starting salary depending on experience

Application forms and further particulars are available from Mr F Morley, Agricultural Research Council, 160 Great Portland Street, London W1N 6DT, to whom completed forms should be returned by August 20, 1973 (180)

APPLICATIONS ARE INVITED FROM recent Ph D graduates for a post-doctoral appointment in the Departments of Urology and Microbiology, Queen's University, Kingston, Ontario, Canada The appointee would participate in investigations into urinary tract infection Experience in Clinical Microbiology a strong asset Appointment for one year in the first instance with renewal if progress satisfactory Salary range $10 000 to $12,000 per annum, according to experience —Applications with curriculum vitae and names and addresses of three referees, to Dr Paul Chadwick, Department of Microbiology, Queen's University, Kingston, Ontario, Canada (173)

Graduate Biochemist or Chemist

Shell Research Limited, Sittingbourne, Kent, have a vacancy for a young graduate biochemist or chemist in the Metabolic and Environmental Chemistry Section of the Chemical Toxicology Division of their Tunstall Toxicological Laboratory

The work will involve a study of the metabolism of foreign compounds in animals and of the mechanisms involved There will be extensive use of radioisotope techniques The studies of the elimination, retention and metabolic products of the foreign compound will be complemented by studies of the location and mechanism of action of the enzymes involved in the detoxification reactions The candidate selected will be expected, in due course, to supervise the team undertaking this work and will report to the Section Leader

This post would suit a young graduate with a good Honours degree in Biochemistry and, possibly, with an M Sc or Ph D Chemistry graduates or postgraduates will also be considered if their studies have involved a substantial amount of animal biochemistry The level of appointment will depend on background and experience, and the salary offered will be competitive

Please write, giving brief details regarding personal background and experience, to Shell Research Limited, Recruitment Division, PNEL/31 (N), Shell Centre, Waterloo, London, SE1 7NA

(188)

Biochemical Technical Assistant

Shell Research Limited, Sittingbourne, Kent, have vacancies for biochemical technical assistants in the Physiological Chemistry Section of the Chemical Toxicology Division of their Tunstall Toxicological Laboratory

The candidates selected will join a team studying the mechanism of the interaction of foreign compounds with biochemical systems in mammals

Ideally, candidates should be in possession of HNC – Applied Biology or equivalent However, practical experience in some aspects of animal biochemistry, enzymology and subcellular fractionation is essential, while experience with radioisotopes and chromatographic techniques is desirable and experience and ability are, therefore, considered more relevant than qualifications The level of appointment will depend on background and experience, and the salary offered will be competitive

Please write or telephone for an application form, addressing enquiries to Shell Research Limited, Personnel Division (O), Sittingbourne, Kent, ME9 8AG (Telephone Sittingbourne 4444, Extension 203)

(189)

Northern Ireland Civil Service

Applications are invited for the following permanent and pensionable post in the Plant Pathology Division of the Ministry of Agriculture

Plant Virologist

To conduct research on plant virus diseases with particular reference to diseases of grass, cereal and horticultural crops

The person appointed may be required to undertake teaching duties in the Department of Mycology and Plant Pathology, Faculty of Agriculture and Food Science, Queen's University, Belfast

Appointments may be at SSO, HSO or SO level

QUALIFICATIONS:

SSO—normally over 25 and under 32 years of age with a good Honours Degree in a scientific or agricultural discipline pertinent to plant pathology with at least 4 years' postgraduate experience in plant virology,

HSO—under 30 years of age with a good Honours Degree as above and at least 2 years' relevant postgraduate experience,

SO—under 27 years of age with a good Honours Degree as above

SALARY SCALES: SSO £2,615—£3,640 HSO £2,076—£2,667; SO £1,318—£2,177

Grading and entry point to salary scales will be related to qualifications and experience

Application forms and further details may be obtained from Recruitment Branch, Civil Service Management Division, Clarendon House, Adelaide Street, Belfast BT2 8ND (telephone 44300, ext 26) Completed applications must be returned so as to arrive not later than 23rd August 1973, quoting Ref SB 165/73/N

(209)

Toxicity Scientist

The Board's extended laboratories include a toxicity testing unit The Toxicity Scientist will be expected to set up, record and interpret tests relating to both the freshwater and marine environments This is a new post offering a considerable challenge Applicants should have a good basic knowledge of biology and chemistry, and preferably have previous experience in toxicity testing animal pathology or physiology

The post is superannuable Salary will be within the range £1,689-£2,475 per annum

Applications, stating age, qualifications and experience, together with the names and addresses of two referees, should be submitted to the Director,
Rivers House, Murray Road, East Kilbride
Glasgow G75 0LA, not later than
August 31, 1973 (244)

NEW ZEALAND
MINISTRY OF AGRICULTURE & FISHERIES

Applications are invited for the undermentioned vacancy

SCIENTIST (BIOCHEMIST, PARASITOLOGIST OR IMMUNOLOGIST)

WALLACEVILLE RESEARCH CENTRE, UPPER HUTT

Salary Payable up to NZ$8,997 depending on qualifications and experience Further promotion is possible on merit up to NZ$12,127

Duties Member of a team studying the host-parasite relationships of the cestodes with particular reference to hydatidosis and cysticerosis, in man and animals

Appointee would undertake a programme leading to the characterization of functional antigens, in relation to immunity, diagnosis, and epidemiology of cestode infection

The successful applicant will be stationed at Upper Hutt near Wellington, North Island

Qualifications Desired B Sc (Honours), M Sc, or Ph D

Passages Fares for appointee and, if married, his wife and family, will be paid

Incidental expenses Up to £55 for a single man and £183 for a married can can be claimed to cover the cost of taking personal effects to New Zealand

Application forms and general information are available from the High Commissioner for New Zealand, New Zealand House, Haymarket, London SW1Y 4TQ, with whom applications will close on **September 28, 1973.**

Please quote reference B13/2/201/3311 when enquiring (211)

NORTH STAFFORDSHIRE POLYTECHNIC
CERAMICS DEPARTMENT,
STOKE-ON-TRENT

RESEARCH ASSISTANTS

There are vacancies in the Department for research into problems connected with Ceramic Technology Candidates will be expected to work for higher degrees (M Phil or Ph D) of C N A A and should, therefore, have at least second class honours degrees in ceramics or natural science, or equivalent professional qualifications

The appointments will be reviewed annually, but will normally last for three years

Salary £1,209 per annum (under review)

Further particulars can be obtained from the Head of the Ceramics Departments

Applications, together with curriculum vitae and the names and addresses of not more than two persons to whom reference may be made, should be sent within two weeks of the appearance of this advertisement to The Deputy Director (Staffing), North Staffordshire Polytechnic, College Road, Stoke-on-Trent Staffs ST4 2DE (247)

FANCY A CHANGE

We have vacancies galore at every grade in the scientific field, including marketing

For further details, write or telephone

WALBROOK APPOINTMENTS,
116 HIGH HOLBORN, LONDON, W C 2
Tel 01-405 8787

(3)

UNIVERSITY
OF DUBLIN
Trinity College

SCHOOL OF VETERINARY MEDICINE

JUNIOR LECTURER/ LECTURER IN PHARMACOLOGY

Applications are invited for the above position from suitably qualified candidates A veterinary qualification is desirable but not essential Research experience in an area of interest to veterinary medicine would be advantageous

Salary scales
Junior Lecturer £1,969 by £126 to £2,473
Lecturer £2,617 by £154 to £3,387 by £147 to £3,534 by £140 to £3,674/Bar/£3,814 by £140 to £4,234

Appointment will be made on either of the above scales according to the qualifications and experience of the successful applicant

Marriage and children's allowances are paid

Further particulars and application form may be obtained from

The Staff Secretary,
West Theatre,
Trinity College,
Dublin 2,

who will receive completed applications up to September 10, 1973 (206)

THE UNIVERSITY OF MANCHESTER INSTITUTE OF SCIENCE AND TECHNOLOGY

CONTROL SYSTEMS CENTRE

LECTURER

The Centre is an interdisciplinary organization having strong links with the Engineering, Mathematics and Computation Departments of the Institute It has excellent computing facilities for control studies and plays a leading part in the development of multivariable control theory

Applicants should have experience of applying control in industry and an interest in one or more of the following areas is desirable, but not essential theory of multivariable systems, algebraic theory of control systems, nonlinear systems hierarchial control, computer-aided design, industrial application of control

Commencing salary will be in the scale £1,929 to £4 548 with superannuation under F S S U

Requests for application forms and conditions of appointment, quoting Reference Number CSC/346/A, should be made to the Registrar U M I S T, Sackville Street, Manchester M60 1QD, to be returned not later than September 14, 1973 (144)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF MICROBIOLOGY

Applications are invited for the post of RESEARCH ASSOCIATE from graduates in Microbiology, Biochemistry or Chemistry, tenable for two years, from October 1, 1973 The post involves work on mechanisms of mycotic infections in animals

Starting salary £1,569 per annum plus F S S U

Applications (3 copies) naming three referees by August 16, 1973, to the Assistant Registrar(S), P O Box 363, Birmingham B15 2TT, from whom further details may be obtained Please quote reference No 2 (141)

Overseas Appointment

This appointment is wholly financed by the British Government under Britain's programme of aid to the developing countries.

Nigeria

JUNIOR TREE PHYSIOLOGIST

To work in a team on a research project on Tree improvement of a selection of West African Hardwoods Applicants preferably under 30 years of age, who should normally be citizens of, and permanently resident in the UK, should possess postgraduate qualifications in an appropriate biological science, with specific interest and preferably expertise in the physiology of root initiation and of flowering and seed production in woody plants Tropical experience would be an advantage Initial appointment for 18 months with the possibility of renewal of a further 18 months

SALARY, subject to UK income tax, in range of £2,000–2,750 pa plus a variable tax free overseas allowance in range of £925–1,760 pa

Other benefits include free family passages, paid leave, children's education allowances and free accommodation and medical attention

For full details, application form and booklet about Nigeria, please apply giving age and brief details of qualifications and experience to:-

Appointments Officer,
Foreign and Commonwealth Office,
Overseas Development
Administration
Room E301 Eland House, Stag Place,
London, SW1E 5DH

(175)

UNIVERSITY OF WAIKATO

HAMILTON, NEW ZEALAND

ACADEMIC VACANCIES

The University has vacancies for LECTURERS in the following fields from February 1, 1974

Computer Science Applicants may have interests in any of the fields of Computer Science with special consideration given to applicants whose research interests are in the fields of operating systems, formal languages, time sharing systems or in the application of computing to business or industrial systems

Mathematics Applicants should be qualified to teach Numerical Analysis and Mathematical Techniques at least at undergraduate level Preference will be given to applicants with research experience in Numerical Analysis, Statistics, Operational Research or Applications of Mathematics to Environmental Studies

The appointments will be made at a suitable step on the scale of salaries for Lecturers in New Zealand universities The scale is in seven steps currently covering the range $NZ5,862 to $7,497 per annum, but if past practice is followed an increase of 8 2 per cent following a ruling rates survey will be made shortly

Conditions of Appointment and details of the application procedure for all positions are available from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572), or from the Registrar, University of Waikato, Hamilton, New Zealand

Applications close on **August 31, 1973**

(202)

ADVISER IN SOIL SCIENCE

Applications are invited for the post of Advisory Officer in the Soil Science Department from graduates in an appropriate discipline The successful candidate will be required to take part in the advisory and development work in the East of Scotland area and may be expected to take a small part in the teaching programme of the Department

The appointment will be made on one of the following salary scales according to qualifications and experience

Grade III	£2,087-£3,640
Grade IVA	£1,499-£1,925

F S S U applies

Further particulars and application form from the Secretary, The Edinburgh School of Agriculture, West Mains Road, Edinburgh EH9 3JG (242)

UNIVERSITY OF GLASGOW

DEPARTMENT OF CHEMISTRY

Applications are invited for a POSTDOCTORAL RESEARCH ASSISTANTSHIP, sponsored by the Science Research Council, for work on the chemistry of electrophilic C-nitroso-compounds The appointment will be for one year, commencing October 1, 1973, at the first or second points on the university lecturer's salary scale

Applications with the names of two referees should be sent to Professor G W Kirby Department of Chemistry, University of Glasgow, Glasgow G12 8QQ (156)

GRADUATE
for
BIOLOGICAL CONTROL

A graduate micro-biologist, or pharmacist who has specialised in micro-biology, is required to take charge of 4 assistants in a section of our Biological Control Department

The work includes monitoring of factory hygiene, drug screening for anti-microbial activity, challenge tests on new formulations and developing methods for quality control Experience of this type of work in the pharmaceutical or allied industry would be an advantage

We offer a competitive starting salary together with a range of fringe benefits which include participation in the profitability of the Glaxo Group, of which we are Members

Please write in confidence to A E Harvey

ALLEN & HANBURYS LTD
Priory Street
Ware Herts
Tel: Hertford 4567

(240)

THE QUEEN'S UNIVERSITY OF BELFAST

DEPARTMENT OF BOTANY

Applications are invited from persons prepared to give teaching assistance for the Department of Botany for one year from October 1, 1973 Preference will be given to candidates with an interest in some aspect of plant ecology It is anticipated that the salary will not exceed £1,923 per annum Applications should be received by August 17, 1973

Further particulars may be obtained from the Senior Assistant Secretary (Personnel), The Queen's University of Belfast, Belfast BT7 1NN, Northern Ireland (Please quote Ref 73/N)

(167)

GLASSHOUSE CROPS RESEARCH INSTITUTE

has TWO vacancies in the PLANT BREEDING DEPARTMENT

(1) HSO/SSO for work on flower breeding Candidates should have a good honours degree in a biological subject with specialization in genetics and physiology of higher plants, and at least two years' postgraduate experience (HSO) or four years' postgraduate research (SSO) Salary scale £2,076 to £2,667 (HSO) or £2,615 to £3,640 (SSO) plus non-pensionable allowance to offset superannuation contributions

(2) SO/HSO for work on glasshouse vegetable crops Good honours degree required in a biological subject with specialization in genetics and plant pathology Salary scale £1,590 to £2,177 SO, £2,076 to £2667 (HSO) plus non-pensionable allowance

Further particulars from Secretary of the Institute, Worthing Road, Rustington, Littlehampton, Sussex, to whom applications with the names and addresses of two referees should be sent before August 31, 1973 (169)

UNIVERSITY OF SIERRA LEONE FOURAH BAY COLLEGE

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN MECHANICAL ENGINEERING Appointee will be required to teach courses in one or more of the following subjects of degree level Thermodynamics, Fluid Mechanics, Applied Mechanics, Machine Design and Drawing Salary scales (under review) (a) Le4,550 to Le5,400 per annum, (b) Le2,400 to Le4,740 per annum (£1 sterling=Le2) The British Government may supplement salary in range £950 to £1,600 per annum (sterling) for married appointee or £350 to £1,000 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages F S S U Family passages, various allowances regular overseas leave

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than September 7, 1973, to the Secretary, University of Sierra Leone, Private Mail Bag, Freetown, Sierra Leone Applicants resident in U K should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT Further particulars of this appointment may be obtained from either address

(150)

HILL FARMING RESEARCH ORGANISATION

Applications are invited for an ASSISTANT SCIENTIFIC OFFICER to assist with chemical analysis of soil, plant and animal samples and with photographic work

Qualifications School leaving certificate with passes in four subjects including English and Chemistry Some experience in photography would be an advantage

Salary £675 (age 16) to £1,612, with entry according to age, plus 5½ per cent non-superannuable allowance Entry at age 25 or over—£1,397 Superannuation

Application forms and further particulars may be obtained from the Secretary, Hill Farming Research Organization, Bush Estate, Penicuik, Midlothian EH26 0PH Please quote Ref A/6/183 Closing date August 31, 1973 (195)

PUBLISHING

The Clarendon Press has a vacancy for a subeditor to work on science books at undergraduate level and above A degree in science is essential and relevant editorial experience is desirable

Salary £1,550 plus (12 by £87) to £2,594

Please apply in writing to

The Secretary (KB),
Clarendon Press,
Walton Street,
Oxford

Closing date September 3, 1973 (215)

UNIVERSITY OF ABERDEEN

TWO POSTS OF POSTDOCTORAL RESEARCH FELLOW IN BIOCHEMISTRY

Applications are invited from graduates in Biochemistry or an applied discipline for above posts to participate in projects with Dr W J Harris

Post one is concerned with the study of the DNA repair capacity and immunological relatedness within human skin tumours Applicants should preferably have postgraduate research experience of nucleic acids or tissue culture Post is initially for 1 year but may be renewable for a further two years

Post two is concerned with the molecular mechanism of genetic recombination during meiosis in *Chlamydomonas reinhardii* Applicants should preferably have postgraduate experience in physicochemical properties of nucleic acids or cell fractionation techniques Post supported by S R C for 3 years Salary in range £1,764 to £2,079 with appropriate placing (scale under review) for both posts

Further particulars from the Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by August 25, 1973

(181)

MICROBIOLOGISTS

BEECHAM RESEARCH LABORATORIES

have vacancies for two Microbiologists in their research laboratories at Brockham Park

One of the posts is concerned with the evaluation of the antibacterial activity of new penicillins This post calls for an interest in antibacterial chemotherapy and would be suitable for recently qualified graduates holding a good degree in Bacteriology or Microbiology

The other post is concerned with fundamental aspects of antibiotic action This work involves some biochemical aspects as well as the biology of the effect of antibiotics on bacterial growth and the post offers scope for original work Candidates should recently have taken a degree in Microbiology or Applied Biology or have an H N C in these subjects

A good starting salary will be offered and reviewed regularly Beecham Research Laboratories are part of the Beecham Group and are situated in a pleasant area of Surrey within easy reach of London There are generous fringe benefits, including sick pay, non-contributory pension fund and bonus scheme

Please reply to the Personnel Officer, Beecham Research Laboratories, Brockham Park, Betchworth, Surrey, or telephone Betchworth 3202 (218)

FIELD STUDIES COUNCIL

TUTOR at the Epping Forest Conservation Centre, Essex Single biologist, male or female, willing to help with junior environmental work as well as more advanced classes Duties also include sharing interpretive services to general public Salary £1,101 by £69 to £1,239, plus residential benefits Closing date August 24 Further details and application forms from the Secretary, Field Studies Council, 9 Devereux Court, London WC2R 3JR (230)

MEDICAL RESEARCH COUNCIL

LABORATORY OF MOLECULAR BIOLOGY

RESEARCH ASSISTANT required (Junior Technical Officer Grade) to develop new micro techniques of amino acid analysis and sequence determination

Please apply in the first instance, giving full details of education, qualifications and any relevant experience to the Administrative Secretary, Medical Research Council, Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH (216)

TOXICOLOGISTS

who want to build a stable and satisfying career by joining a small research company which is growing fast, are invited to enquire about several positions in the £2,000-£3,500 p a salary range All of these provide key opportunities arising from our need to expand

A generous non-contributory pension is provided and profit-sharing is envisaged

Please write giving full career details, which will be treated in the strictest confidence, to The Director, Life Science Research, Stock, Essex, CM4 9PE, England

(245)

THE MEDICAL SCHOOL, UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF EXPERIMENTAL PATHOLOGY, RHEUMATISM RESEARCH WING

SENIOR CHIEF TECHNICIAN

(N H S grade)

Senior Chief Technician required to take technical charge of the Rheumatism Research Wing Applicants should hold the F I M L T or equivalent and have experience of laboratory administration Preference will be given to candidates with experience of clinical chemistry, immunology and biochemistry, but a broad biological background and experience of other laboratory disciplines will also be favourably considered Good opportunities are available to proceed to higher qualifications and to partake in research relating to rheumatic and cardiovascular diseases Salary according to age and experience

Applications, stating age, qualifications, previous experience, and the names of two persons willing to provide references to Assistant Secretary (Personnel), University of Birmingham, P O Box 363, Birmingham B15 2TT, quoting Reference 407/A/827 (248)

UNIVERSITY OF ABERDEEN

RESEARCH ASSISTANT IN MEDICAL PHYSICS

Applications are invited for the above post in ULTRASONICS The work involves development of new ultrasonic scanning techniques Candidates should have a good honours degree in Electronic Engineering or equivalent, and preferably some postgraduate experience in a related field Appointment is for two years in first instance and initial salary will be within the range £1,509 to £2,160 or £2,166 to £2,916 with placing according to qualifications and experience

Further particulars from the Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by August 25, 1973 (182)

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF CHEMISTRY

PHYSICIST OR PHYSICAL CHEMIST

A vacancy exists for a Postdoctoral Research Fellow to work in a group using modulated specular reflectance spectroscopy to study a variety of electrode processes

Candidates should have experience in or a sound knowledge of one or more of the following areas surface chemistry or physics, solid state physics, electrochemistry, computing

The salary will be in the range £1,929 to £2,223 with F S S U benefits

Applications with a curriculum vitae and naming two referees should be sent to Dr A Bewick, Department of Chemistry, The University, Southampton SO9 5NH (212)

ST THOMAS'S HOSPITAL

LONDON, S E 1

BASIC GRADE BIOCHEMIST

Applications are invited for the post of Basic Grade Hospital Biochemist in the Department of Chemical Pathology Whitley Council terms and conditions of service Preliminary visit arranged or inquiries to Professor R V Brooks (01-928 9292, ext 2387) Closing date September 1, 1973

Application form from Personnel Officer, 79 York Road, London, S E 1 (239)

UNIVERSITY OF CAPE TOWN

SENIOR LECTURER IN WATER RESOURCES AND PUBLIC HEALTH ENGINEERING

Applications are invited for the post of Senior Lecturer in Water Resources and Public Health Engineering in the Department of Civil Engineering from January 1, 1974 The applicant must hold a Ph D in a field related to the control of water quality An interest in Coordination Chemistry will be a strong recommendation The appointment will be made on the scale R6,300 by R300 to R8,100 per annum plus a pensionable allowance of 15 per cent of basic salary

LECTURERS IN CIVIL ENGINEERING

Applications are invited for two posts of Lecturer in the Department of Civil Engineering from January 1, 1974 Applications will be considered from candidates who are specially qualified in any of the branches of Civil Engineering The appointments will be made on the salary scale R4,800 by R300 to R6,300 per annum plus a pensionable allowance of 15 per cent of basic salary

The starting salary in each case will be determined according to qualifications and experience

Applicants should submit a curriculum vitae, stating present salary, the date on which they could assume duties, and giving the names and addresses of three referees (preferably persons with recent familiarity with the applicant's activities)

Two copies of the application should reach the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (from whom memoranda giving the conditions of service, including transport expenses on appointment, and information on the work of the Department may be obtained) not later than **October 15, 1973** A third copy of the application should be sent direct by airmail to the Registrar University of Cape Town, Private Bag, Rondebosch, Cape Town, South Africa, by the same date

Appointment will be subject to a satisfactory medical examination

The University reserves the right to appoint a person other than one of the applicants, or to make no appointment (227)

PROFESSOR OF ZOOLOGY

Applicants should be holders of Ph D degree, followed by considerable teaching experience at University level as well as conducting original research He or she should preferably have had experience in the running of a University Department and supervising postgraduate student research Salary £3,600 by £156 to £4,380 per annum Terms of service include subsidised housing, membership of a Senior Staff Superannuation Fund or F S S U, and of a non-contributory medical scheme Expatriate appointments are on tours, each of two years, renewable, and include passages for up to 5 adults on appointment, termination and between tours

Applicants should give names and addresses of three academic referees and at the same time ask them to send their references direct to the Registrar without delay Written applications (six copies) giving full details of curriculum vitae including fields of specialization, age, present post, marital status, etc, etc, should be addressed to The Registrar, Kenyatta University College, P O Box 43844, Nairobi, Kenya, to reach him not later than August 20, 1973 (214)

UNIVERSITY OF BRISTOL

DEPARTMENT OF THEORETICAL CHEMISTRY

LATTICE DYNAMICS OF AMORPHOUS SOLIDS

Applications are invited for a postdoctoral Research Assistantship supported by S R C to continue an active theoretical investigation of the thermal expansion of vitreous silica and related crystalline and amorphous solids The investigation is associated with experimental work in the Department of Physical Chemistry, it also includes a study of vibrational excitations in quartz in association with experimental work at the Institut Laue-Langevin at Grenoble

Funds are available until August 31, 1974, and will then depend upon whether the period of the original grant from S R C can be extended

Salary on scale £1,764 to £2,238 (£1,929 to £2,388 with effect from October 1, 1973) depending upon age, qualifications and experience

Applications in writing and giving the names of two referees should be sent to Dr T H K Barron Department of Theoretical Chemistry, University of Bristol, Cantock's Close, Bristol BS8 1TS (220)

UNIVERSITY COLLEGE CARDIFF

ASSISTANT EXPERIMENTAL OFFICER/ EXPERIMENTAL OFFICER

in the Department of Botany Salary range £1,764 to £2,874/£3,033 to £3,351 Duties to commence October 1, 1973 Applications together with the names of two referees, should be forwarded to the Registrar, University College, P O Box 78, Cardiff CF1 1XL, no later than August 31, 1973 Please quote 0883 (221)

UNIVERSITY OF BRISTOL

LONG ASHTON RESEARCH STATION

SCIENTIFIC OFFICER

required in the Biometrics Section to assist research workers in the analysis, interpretation and presentation of experimental data on fruit and other plants, and in the development of mathematical models

Minimum qualifications pass degree, H N C or equivalent in Statistics or Mathematics, or in a Biological subject with some Mathematical ability

Appointment in the Scientific Officer grade (£1,318 to £2,177), commencing salary according to qualifications and experience Optional superannuation scheme with allowance to offset contributions

Applications to the Secretary, Long Ashton Research Station, Long Ashton, Bristol BS18 9AF, by September 7, 1973 (207)

UNIVERSITY OF NEW SOUTH WALES

SCHOOL OF MATHEMATICS

LECTURER

Salary $A8,698 range $A11,982 per annum Commencing salary according to qualifications and experience

For the Department of Applied Mathematics Distinguished academic record required Qualifications in mathematical physics, particularly in the area of statistical mechanics or solid state physics advantageous

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

Applications close in Australia and London on **September 7, 1973.** (225)

UNIVERSITY OF LEICESTER

A vacancy exists for a GRADE 4 TECHNICIAN in the Department of Zoology The responsibilities of the appointee will be diverse and include organization of ecological courses, including preparation of materials and maintenance and construction of equipment, also assisting graduate students Preference will be given to applicants with a knowledge of computer techniques, and an additional advantage will be experience in freshwater ecology Qualifications should include I S T (Advanced), or H N C, or H N D Salary (Grade 4) £1,728 to £2,028

Applications, together with the names of two referees, should be sent to Dr J A Bullock, Senior Lecturer in Ecology, Zoology Department, University of Leicester, Leicester LE1 7RH, before August 20, 1973 (210)

MEDICAL RESEARCH COUNCIL

SCIENTIST required for the Secretariat of the Committee on Protection against Ionising Radiations Duties include the reporting and organising of meetings, appreciation of current literature on a wide variety of topics in biology, medicine, and physics There would be opportunities for theoretical, experimental or epidemiological work on the relationship between effects and dose of ionising radiation The successful candidate would be located at the Radiobiology Unit at Harwell and would enjoy M R C salary scales and conditions of service

Applications should be addressed to
The Administrator,
M R C Radiobiology Unit,
Harwell, Didcot Berks ,
to reach him by August 24, 1973 Please quote Reference FDB/33 (249)

M R C CLINICAL RESEARCH CENTRE

(NORTHWICK PARK HOSPITAL)
WATFORD ROAD, HARROW,
MIDDLESEX HA1 3UJ

There is a vacancy for a GRADUATE (Honours degree essential) in biochemistry/microbiology for research involving gas chromatography of bacteria and products of bacterial metabolism Knowledge of bacterial metabolism is essential experience of gas chromatography is desirable not but essential The appointment is for 3-5 years, and the salary, which is dependent upon age and experience, will be within the range £1,668 to £3,192 plus £162 London Allowance a year

Further particulars and application forms may be obtained from Mrs J Tucker-Bull Closing date September 7 Please quote Reference 116/1 (241)

UNIVERSITY OF QUEENSLAND

AUSTRALIA

LECTURER IN BIOCHEMISTRY

Qualifications Minimum qualification a Ph D in Biochemistry and a strong commitment to both teaching and research Preference will be given to applicants whose research interests lie in the area of plant biochemistry

Salary $A8,698 to $A11,982 per annum

Other benefits Superannuation similar to F S S U , housing assistance, study leave, and travelling and removal expenses

Additional information and application forms are obtainable from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (Tel 01-387 8572)

Applications close in London and in Brisbane on **September 28, 1973.** (204)

UNIVERSITY OF GLASGOW

LECTURESHIP IN MICROBIOLOGY

Applications are invited for a Lectureship in Microbiology in the Faculty of Science The salary placement will initially be at the lower end of the Lecturers' scale of £1,929 to £4 548 per annum F S S U

Preference will be given to applicants with experience in microbial biochemistry and with research interests in that area or in microbial genetics or microbial pathogenicity

Applications (eight copies) should be lodged not later than October 15, 1973, with the undersigned from whom further particulars may be obtained

In reply please quote Ref No 3334 M

ROBT T HUTCHESON,
Secretary of the University Court
(231)

CHARING CROSS HOSPITAL

FULHAM PALACE ROAD, LONDON W6 8RF

Applications are invited for a new post of IMMUNOLOGIST in the Department of Medical Oncology The person appointed will be in charge of a small group which will establish and apply cellular immunological methods for tumour associated antigens and will work in conjunction with an established group of protein chemists

Applicants should be post-doctoral and have experience of cell mediated techniques and preferably in the field of tumour immunology Grade Clinical Lecturer, Lecturer or Senior Biochemist, according to experience and qualifications

Application forms from Miss J M Peggs, Personnel Department, Charing Cross Hospital, to be returned by September 3 All enquiries to 01-748 2050, Ext 2993 (233)

A vacancy exists for a LABORATORY TECHNICIAN in the Department of Histopathology, who possesses the Higher National Certificate in histopathology or Junior Technical Grade B who possesses the Ordinary National Certificate Telephone enquiries to Mr Florio (01-486 0824 Ext 146) and written applications to House Governor, National Heart Hospital, Westmoreland Street, W 1, within 14 days (149)

UNIVERSITY OF LONDON

BRITISH POSTGRADUATE MEDICAL FEDERATION

INSTITUTE OF LARYNGOLOGY AND OTOLOGY

330/336 GRAY'S INN ROAD, LONDON W C 1

Two-year Medical Research project, " Binaural hearing " (grant-aided) Salary £1,449 to £1,608 per annum to a science graduate (with good honours degree in electrical engineering, physics, physiology or psychology) available to commence not later than October 1, 1973

Applications with full curriculum and naming referees to the Secretary-Administrator (N), Institute of Laryngology and Otology, 330/336 Gray's Inn Road, London W C 1 Closing date, August 31, 1973 (237)

UNIVERSITY OF LEICESTER

BOTANICAL LABORATORIES

RESEARCH ASSISTANT

Applications are invited for an appointment as Research Assistant to work on dark carbon dioxide fixation and the regulation of photosynthetic carbohydrate metabolism in higher plants Candidates should possess a degree in a biological science and an interest in plant physiology and biochemistry

The appointment will be for one year in the first instance but will be renewable up to a period of three years Initial salary will be £1,209 (under review) or at an adjusted level in the case of a candidate who registers for a higher degree

Applications, together with the names of two referees, should be sent to Dr W Cockburn, Botanical Laboratories, University of Leicester, Leicester LE1 7RH Closing date September 15, 1973 (235)

FULMER RESEARCH INSTITUTE LTD ,

STOKE POGES, SLOUGH SL2 4QD
BUCKINGHAMSHIRE

Young GRADUATE PHYSICAL CHEMIST required for precision thermochemical work in inorganic chemistry Good experimental ability is needed

Satisfactory results will be published and the nature of the work can be seen from publications which have appeared in, for instance, Transactions of the Faraday Society, with P Gross as senior author

Applications to the Director of Research (170)

GENERAL HOSPITAL

ROTHWELL ROAD, KETTERING
NORTHANTS NN16 8UZ

BIOCHEMIST (Principal Grade) required This is a new appointment in an expanding department The new laboratory will shortly be completed and is due to be commissioned early in 1974 It serves a population of 200,000 and is well equipped The successful candidate will be responsible for running the Chemical Pathology Laboratory and will work in conjunction with the Consultant Pathologist He should have a wide experience in hospital biochemistry The hospital may be visited by arrangement with Dr P S Andrews, telephone 0533 4996

Further particulars and applications, together with the names and addresses of two referees, to the Acting Group Secretary (238)

RESEARCH TECHNICIAN REQUIRED FOR two-year appointment under S R C project for work on microbial transformation of sugars Applicants should have experience in microbiological or biochemical techniques Salary scale (grade 3) £1,539 to £1,794 plus £175 London Weighting —Applications to Professor S J Pirt (N), Queen Elizabeth College (University of London), Campden Hill Road, Kensington W8 7AH (236)

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UNIVERSITY HOSPITAL OF WALES

DEPARTMENT OF HAEMATOLOGY

A Scientific Officer

to assist in research and development within the Department The Department provides a comprehensive service for the investigation of disorders of the blood This is a rapidly expanding field which calls for the development and evaluation of new biological and biochemical methods including the application of quality control and data processing techniques

Applicants should be science graduates with an interest in laboratory methodology and the ability to work independently on specified projects

Salary £1,566 for 1st or 2nd class honours graduates, £1,278 for other graduates (rising by annual increments to £2,370)

Further particulars can be obtained from Professor A Jacobs, Department of Haematology, Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN, to whom applicants should direct all enquiries

(224)

UNIVERSITY COLLEGE OF NORTH WALES

BANGOR

MARINE SCIENCE LABORATORIES, MENAI BRIDGE

Applications are invited for a post as

DEMONSTRATOR

Applicants for this post should be honours graduates in Chemistry, Biochemistry or Microbiology

The initial appointment will be for one year commencing as soon as possible after October 1, 1973, with a possibility of renewal for a further period of two years

The salary will be £1,494 per annum plus F S S U benefits

Applications (two copies), giving details of age, qualifications and experience together with the names and addresses of two referees should be sent not later than August 28, 1973, to the Secretary and Registrar University College of North Wales, Bangor, from whom further particulars may be obtained (163)

UNIVERSITY OF ABERDEEN

DEPARTMENTS OF CHEMICAL PATHOLOGY AND MEDICAL PHYSICS

BIOCHEMIST with postgraduate research experience required to investigate origin of spin resonance signals from human tissue samples, working with small team from other disciplines Appointment supported by grant for two years in first instance Salary on Research Assistant scale—£1,509 to £2,160 or £2,166 to £2,916 with placing according to age, qualifications and experience

Further particulars from the Secretary, The University, Aberdeen, with whom applications (3 copies) should be lodged by August 25, 1973 (229)

MURDOCH UNIVERSITY

VETERINARY SCHOOL

CHAIR IN DIVISION OF VETERINARY BIOLOGY

CHAIR IN DIVISION OF APPLIED VETERINARY MEDICINE

Applications are invited for two senior posts

Chair in Division of Veterinary Biology The division will encompass anatomy, biochemistry, physiology, nutrition, genetics, pharmacology toxicology, microbology, parasitology and general pathology The appointee will be expected to demonstrate senior academic qualifications and experience in one of these fields An interest in achieving co-operative interaction among these disciplines backed up by administrative flair would be a distinct advantage The major role will be to develop these areas basic to the professional study of veterinary science and to broader interests within the new university Participation in planning first-year programmes leading to biological, veterinary and related careers would be an additional responsibility Close co-operation with the applied veterinary medicine group in developing an overall veterinary studies programme would also be expected This post can start early in 1974

Chair in the Division of Applied Veterinary Medicine The division will encompass diagnostic and clinical pathology, epizootiology and public health, animal production and preventive veterinary medicine, veterinary medicine, veterinary surgery and obstetrics, anaesthesiology, theriogenology, radiology, state veterinary medicine and jurisprudence Applicants should demonstrate senior qualifications and experience appropriate to one of these fields backed up by administrative ability This appointment will carry responsibility for developing the component disciplines and planning the programme in applied veterinary medicine Development of a satisfactory field instruction programme utilizing regional resources and relating to regional problems will be an important aspect A strong thrust in diagnostic and preventive medicine is envisaged for the agricultural applications along with a high standard of clinical training for equine and pet practice Co-operation with and utilization of the resources available in Veterinary Biology will be expected in developing a forward-looking programme having a sound academic foundation This post will be funded from early 1975

The Head of the Veterinary School is Dr R H Dunlop, from the University of Saskatchewan First-year courses will begin at Murdoch in February 1975 and the professional curriculum will start in 1976 The enrolment in the Veterinary School will be restricted to a maximum of 48

The professorial salary is $A19,102 per annum

Further information about Murdoch University and the conditions of these appointments may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF, or from the Secretary, Murdoch University, Box 139, Post Office Nedlands, Western Australia, 6009

Applications will close on **October 1, 1973**

(228)

UNIVERSITY OF MALAYA

FACULTY OF AGRICULTURE

Applications are invited for the post of Lecturer/Assistant Lecturer in the Faculty of Agriculture in the following fields listed below Candidates should have a good honours degree in Agricultural Science or Basic Science with higher degree qualifications in the appropriate areas listed below Subject to academic suitability and experience, preference will be given to candidates who are competent in Bahasa Malaysia (Malay)

Agricultural Education/Extension especially rural sociology

Agricultural Economics Farm Management and Production Economics

Soil Science Soil Survey and Soil Fertility

Animal Science Food Science

Note A new University of Agriculture has been set up in 1972 and our present Faculty of Agriculture will cease its undergraduate teaching programme as from 1976 In view of this, all future offers of appointment to the Faculty of Agriculture will be made either by the University of Malaya or the University of Agriculture University of Malaya will only offer appointments on short-term contracts whereas the University of Agriculture may offer appointments either on short-term contract or on initial contract with prospects of permanency

Emoluments (approximate sterling equivalents per annum) are

(i) Salary scales Lecturers, £1,524 by £73 to £1,962/£2,035 by £81 to £2,441, Assistant Lecturers, £1,330 by £65 to £1,460

(ii) In addition a Variable Allowance is at present payable at the following rates 35 per cent of basic salary subject to certain maxima depending on marital status, minimum £243 per annum, maximum £649 per annum

(iii) Supplementary Housing Allowance £503 per annum

Medical benefits are provided under the Medical Services Scheme of the University

Further particulars, details of superannuation and application forms are obtainable from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

The closing date for the receipt of applications is **September 3, 1973.** (226)

FELLOWSHIPS AND STUDENTSHIPS

UNIVERSITY OF DUNDEE

DEPARTMENT OF BIOCHEMISTRY

POSTDOCTORAL RESEARCH FELLOWSHIP

Applications are invited for the above position from persons who hold or expect shortly to hold a Ph D degree in biochemistry The research will form part of a programme to study the structure and regulation of the multienzyme complex which controls glycogen breakdown and synthesis, and is supported by grants from the Science Research Council and the British Diabetic Association Candidates should have experience in protein chemistry, enzymology, or carbohydrate chemistry, and have a strong interest in enzyme regulation The position is initially for 18 months and may be taken up at any time between October 1973 and February 1974 The salary will be not less than £1,764 per annum plus F S S U benefits

The Biochemistry Department is housed in a new Medical Sciences Institute and has excellent facilities and space for research Applications, containing the names of three referees, should be sent by September 1 to Dr Philip Cohen, Biochemistry Department, Medical Sciences Institute, The University, Dundee DD1 4HN, Scotland, from whom further details may be obtained

Please quote Reference EST/59/73J

(243)

UNIVERSITY OF KENT AT CANTERBURY

RESEARCH FELLOW IN CHEMISTRY

Applications are invited for an SRC Post-doctoral Research Fellowship tenable for 2 years from October 1, 1973, for a study of radical anions by mass spectrometry and electron spin resonance spectroscopy in collaboration with Dr J F J Todd Starting salary £1,929 to £2 058

Application forms and details may be obtained from the Assistant Registrar, Faculty of Natural Sciences, Chemical Laboratory, The University, Canterbury CT2 7NH, Kent Please quote ref A32/73 Closing date for applications, August 24

(153)

UNIVERSITY OF WARWICK

POST-DOCTORAL FELLOWSHIP IN MOLECULAR SCIENCES

Applications are invited for an S R C Post-doctoral Fellowship for work on the photochemistry of metal ions and complexes including organometallic systems, principally by laser flash photolysis and cryogenic i r methods and in collaboration with Drs A Cox and T J Kemp Initial salary £1,929 or £2,058 per annum depending on age and experience The vacancy is for two years from October 1, 1973

Written applications, naming two referees, should be sent to the Academic Registrar, University of Warwick, Coventry CV4 7AL, as soon as possible Please quote Ref No 1/Q/73 (219)

KING'S COLLEGE, CAMBRIDGE

Fellowships in Applied Probability Theory in Relation to Population Biology

Applications are invited for Fellowships in the above field, including population and human genetics, ecology, evolutionary theory, demography and stochastic diffusion processes, to be held (from October 1974, or by arrangement) in the King's College Research Centre where computing facilities are available Senior (age limit of 32 years) and Junior (age limit of 28 years and not more than about 3 years research experience) fellowships are available together with an unrestricted fellowship which could be held by a senior worker on sabbatical leave Maximum tenure, 4 years Closing dates October 1, 1973 for senior and open, November 15, 1973 for juniors Details of stipend accommodation research facilities, etc from The Convener, King's College Research Centre, King's College, Cambridge CB2 1ST, England (18)

UNIVERSITY OF READING

DEPARTMENT OF FOOD SCIENCE

Applications are invited from graduates in Chemistry or Biochemistry for a FOSS ELECTRIC RESEARCH STUDENTSHIP leading to a higher degree The project is concerned with the use of dyes to measure the protein content of foods These techniques are widely employed in the Food Industry and the Department is recognized as a centre for research into their theory and application Among the aspects to be studied in detail will be the nature of the dye-protein interaction which occurs under the conditions employed in these methods

Apply quoting Ref MN 52, with the names of two referees, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH

(140)

UNIVERSITY OF STRATHCLYDE

Department of Biochemistry

SRC RESEARCH STUDENTSHIP

Applications are invited from holders of First or Upper Second Class Honours' Degrees in Biochemistry or associated subject for an SRC Studentship (CASE award in conjunction with ICI Pharmaceuticals Division)

The successful candidate will be engaged in the biochemistry of reproduction involving the effects of prostaglandins on ovarian steroid metabolism

The value of the award will be in accordance with SRC rates Applications with the names of two referees should be sent to Dr J Watson, Department of Biochemistry, University of Strathclyde, Royal College Building, 204 George Street, Glasgow G1 1XW

(194)

THE QUEEN'S UNIVERSITY OF BELFAST

RICHARDSONS ULSTER STUDENTSHIP

Open to graduates in Agricultural Chemistry, Biochemistry or Chemistry with suitable subsidiary subjects, preference being given to applicants of Northern Ireland parentage The holder will undertake research work connected with plant nutrition or the biochemistry of plant growth and may register for a higher degree of the University The work will be carried out in the Agricultural and Food Chemistry Department of the University

The Studentship is tenable up to three years and its value will be £600 in the first year of tenure rising annually by £50 to a maximum of £700 An allowance of up to £150 per annum will be available for approved expenses

Candidates should apply in writing, giving full details of their qualifications, to the Dean of the Faculty of Agriculture and Food Science, Queen's University, Belfast BT9 5PX, by August 24, 1973 (21)

UNIVERSITY OF LONDON INSTITUTE OF PSYCHIATRY

DEPARTMENT OF NEUROLOGY

POSTDOCTORAL RESEARCH FELLOWSHIP

Applications are invited from recently qualified doctorates in biochemistry or pharmacology for a study of the biochemical/pharmacological basis of some drug-induced basal ganglia diseases Suitable candidates should preferably have a knowledge of biogenic amine metabolism and be familiar with current physico-chemical methods of analysis

Salary within the range £1,926 to £2,241 including London allowance renewable annually up to three years

Applications in writing together with a curriculum vitae should be sent to the Secretary, Institute of Psychiatry, De Crespigny Park, Denmark Hill London SE5 8AF from whom further details may be obtained, quoting reference PJ/N (146)

UNIVERSITY OF NOTTINGHAM

DEPARTMENT OF APPLIED BIOCHEMISTRY AND NUTRITION

FOOD SCIENCE LABORATORIES

S R C (C A P S) RESEARCH STUDENTSHIP

Applications are invited from suitably qualified candidates (good Honours degree or equivalent) in physical chemistry or an allied discipline for a C A P S Studentship, in association with Lyons Central Laboratories, directed to the study of freeze thaw change in gels The proposed project involves the application of a number of advanced biophysical techniques to the investigation of a problem of considerable practical importance

Applications (and enquiries) should be sent as soon as possible to J M V Blanshard, Department of Applied Biochemistry and Nutrition, Nottingham University, Sutton Bonington, Loughborough, Leics, from whom further details may also be obtaned

(234)

CHELSEA COLLEGE

UNIVERSITY OF LONDON

CAPS RESEARCH STUDENTSHIP

Applications are invited from suitably qualified candidates for a S R C Research Studentship under the C A P S scheme with the Allen Clark Research Centre of The Plessey Company Limited, Caswell, Towcester, Northants The subject of the research is the study of deep energy levels in silicon and in other semiconductor materials using the method of thermally stimulated currents and other suitable techniques The project continues a previous C A P S scheme which is approaching completion, leaving an instrumental set-up The project is jointly supervised by Professor A K Jonscher at Chelsea College and by a member of the Caswell Laboratories and involves periods of work by the student at Caswell

Applications to be sent to Mrs V Boulton, Chelsea College, Pulton Place, London SW6 5PR

(201)

THE CITY UNIVERSITY

DEPARTMENT OF CHEMISTRY

Applications are invited for a Research Studentship which is available from October 1 1973, for studies of the spontaneous ignition of hydrocarbon-air mixtures with special reference to the application of computer techniques The value of the award will be at least equivalent to that of an S R C Research Studentship and the successful candidate will be able to register for a Ph D degree

Further details may be obtained from Professor C F Cullis Department of Chemistry, St John Street, London EC1V 4PE, to whom applications, together with the names of two referees, should be sent as soon as possible (198)

THE UNIVERSITY OF ASTON IN BIRMINGHAM

RESEARCH STUDENTSHIP available in the field of general endocrinology, to study aspects of pancreas, thyroid and pituitary function in mammals Applications, including curriculum vitae, to Professor A J Matty, Department of Biological Sciences The University of Aston in Birmingham, Gosta Green, Birmingham B4 7ET (196)

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DEPARTMENT OF BIOLOGY

Applications for a research studentship are invited from graduates with 1st or upper 2nd class honours in Plant Physiology or a related subject This is an S R C supported Co-operative Award arranged with the Glasshouse Crops Research Institute, Rustington, Sussex The project will involve work on factors influencing inflorescence and fruit development in glasshouse-grown tomato plants under winter light regimes Candidates will be expected to register for the Ph D degree

Applications (including a curriculum vitae and the names of two referees) should be addressed as soon as possible to Dr D A Morris, Department of Biology, Building 44, The University, Southampton SO9 5NH, from whom further details may be obtained (Tel Southampton 559122, Ext 2032)

(187)

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Further details may be obtained from Dr M Rigby, Queen Elizabeth College, Campden Hill, London W8 7AH (177)

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Applications, with curriculum vitae, and two referees, should be sent to Dr D G Hoare Biology Department, University of York, York, YO1 5DD, as soon as possible (137)

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(15)

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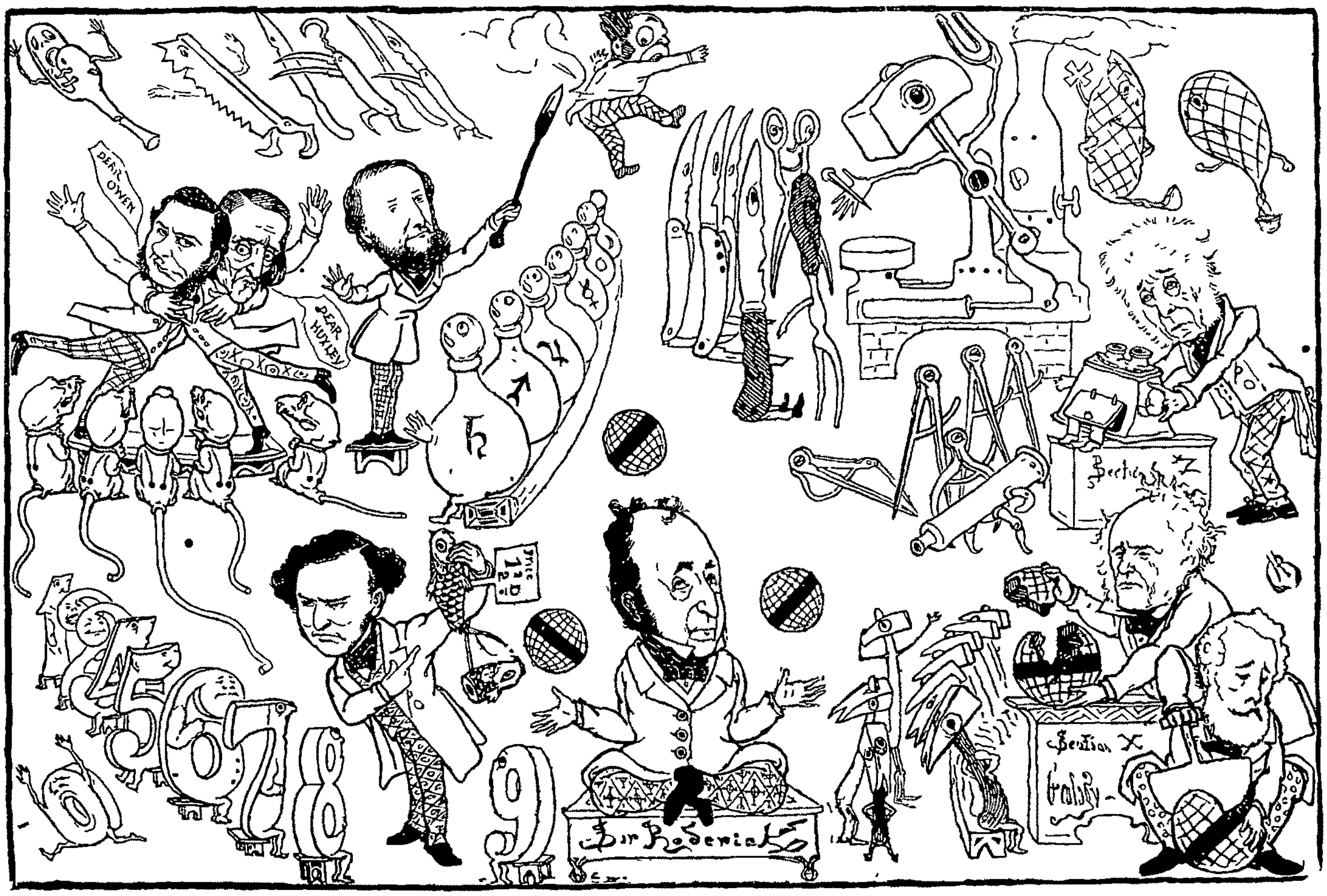

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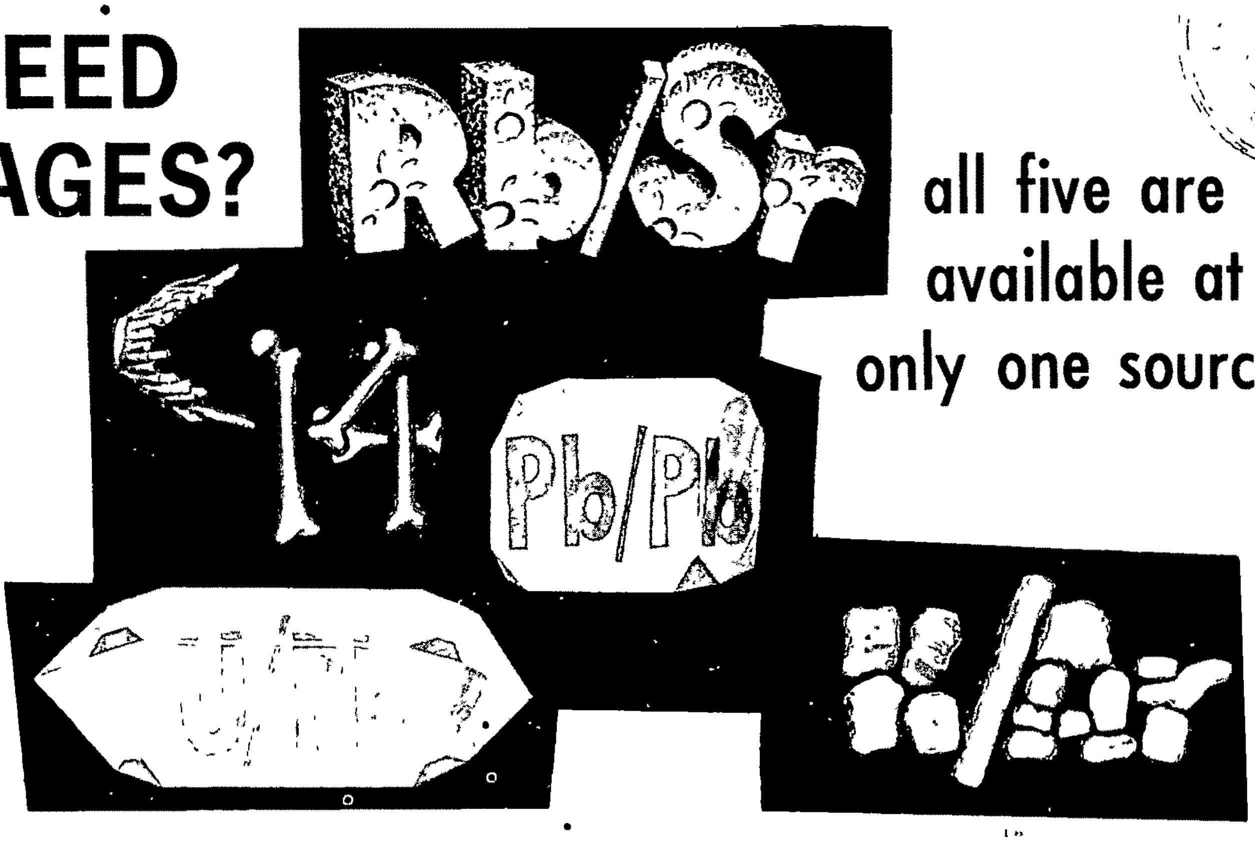
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Disorders of Auditory Function

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This volume comprises an edited version of papers presented at the first British Conference of the British Society of Audiology, held at the University of Dundee from the 14th to 16th July, 1971
The papers read at the conference cover a wide field, the deliberate aim of the organisers being to appeal not only to experts and research workers but to all those concerned clinically with the measurement of hearing The text deals with such interesting aspects as noise-induced hearing loss, the reduction of noise both in industry and in the community and the measurement of hearing loss by subjective and objective methods

Inborn Errors of Metabolism

Report of a symposium on the relation between developmental biochemistry and inborn errors of metabolism

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August 1973, xvi+376 pp., £7.00 0.12.354550.1

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Modern Techniques in Physiological Sciences

Proceedings of an International Symposium on Modern Technology in Physiological Sciences held in Munich, July 1971.

edited by R. Kaufmann, J. F. Gross and E. Wetterer

October 1973, xvi+536 pp., £7 00 0.12.304450.2

This book results from a symposium held at Munich in July 1971 It aims to bridge the information gap which exists between manufacturers and biomedical scientists by publishing contributions from researchers who, in most cases, have already successfully applied new techniques to their own branch of biomedical science Many new approaches for biomedical research are revealed, stemming from recent progress in the physical and engineering sciences

Multivariate Analysis and Psychological Theory

The Proceedings of the Third Banff Conference on Theoretical Psychology held at Banff, Alberta, Canada in September and October 1971

edited by Joseph R. Royce

August 1973, xvi+568 pp., £8.20 0.12.600750.0

Behaviour, especially human behaviour, must surely be the most complex system of events to come under scientific surveillance This volume is concerned with a multivariate approach to the subject, and aims to provide a comprehensive statement on the theoretical implications of multivariate analysis in psychology The contributors believe that there has been insufficient awareness among psychologists of the potential for multivariate theory and this book was stimulated by their concern about the present multivariate-theoretic vacuum hopefully, it will provide a platform upon which to build

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N. Popescu

September 1973, xii+470 pp., £11.50 0.12.561550.7

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Pulsars—Upper limits to pulsed X-ray flux from three pulsars—CRUISE and NEWTON (University College, London)

Next Wednesday's issue will include

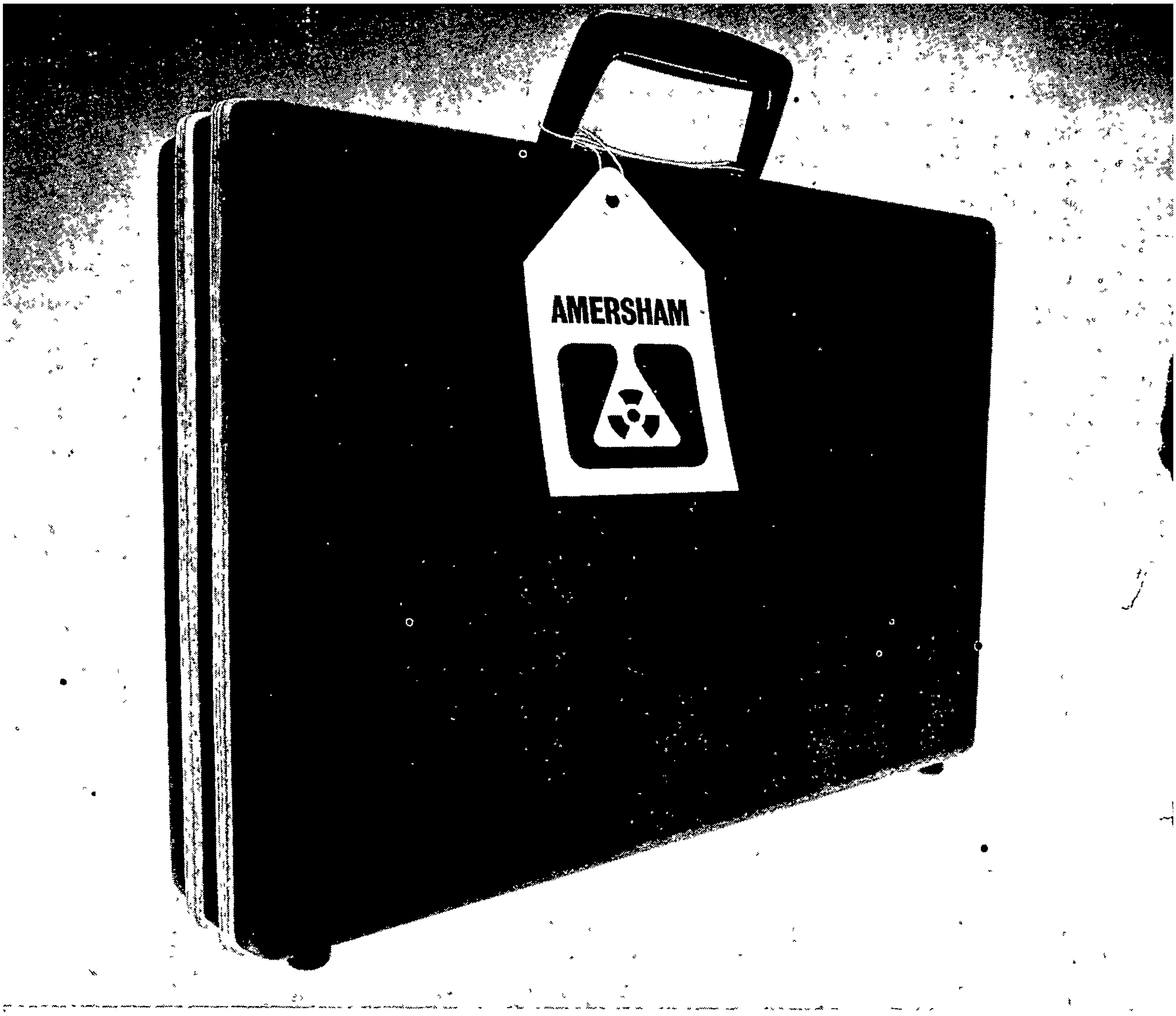
Genetics—Ribosomal protein genes in *Drosophila* mapped—STEFFENSEN (Urbana, Illinois)

Phenylalanine tRNA—Site of aminoacetylation—SPRINZL and CRAMER (Gottingen)

mRNA—Sequence of mRNA for light chains of immunoglobulins—BROWNLEE, CARTWRIGHT, COWAN, JARVIS and MILSTEIN (MRC, Cambridge)

rRNA—Environmentally induced changes in rRNA gene redundancy—TIMMIS and INGLE (Edinburgh)

British Association Conference, Canterbury—the attention of delegates is drawn to the classified page xxxii



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NATURE • Volume 244
AUGUST 17 1973

Sad Case of Dr Zhores Medvedev

DR ZHORES MEDVEDEV's truce with the Soviet authorities has come to an inglorious end What most informed western observers had foreseen and, more than likely, what Dr Medvedev had feared, came to pass By what can be called nothing but trickery Dr Medvedev and his wife were twice summoned to the Soviet Embassy in London last week and during the second visit the true reason for the summons was revealed and Dr Medvedev was informed that his Soviet citizenship had been cancelled and his passport, which he was told belonged to the state, had to be surrendered

In retrospect no one should be surprised by this action, for apart from adding another chapter to the already chequered career of Dr Zhores Medvedev the move is entirely in keeping with the character of the Soviet authorities In recent months *Nature* has more than once taken note that Soviet scientists are being victimized, for all scientists, whether they are practising their professions in the western world or beyond the Iron Curtain, should be concerned when colleagues are being persecuted In this respect it has to be said, in answer to those who have taken *Nature* to task recently for highlighting the fate of Soviet scientists while apparently ignoring the fate of other persecuted intellectuals, that the journal is not a platform for discussing all aspects of human rights Nevertheless *Nature* must take note when scientists, from any country, are persecuted because of their profession Since coming to Britain in January, Dr Medvedev has neither discussed publicly his previous treatment by the Soviet authorities—as well he might have—nor has he in any way criticized his government's policies His one public statement, made in the wake of last week's events, is factual and contains no adverse comment and it is clear that he is still determined to return to the Soviet Union to continue his scientific work It is indeed the duty of his fellow scientists to help him and the question is how best to do this

It is paradoxical that while the Soviet authorities are faced with several dissident Jewish scientists trying to emigrate to Israel, Dr Zhores Medvedev is deprived of the basic human right of being able to return to live in his own country But the Soviet Union was one of the countries which did not vote in favour of the United Nations Declaration of Human Rights and so, presumably, it does not feel bound by the article in the declaration which states that everyone has the right to leave and to return to his own country In the long run it would be a laudable aim to get the Soviet Union to approve this declaration, but in the short term this is not going directly to benefit Dr Medvedev or those potential emigré scientists There is a campaign in progress to help Jewish scientists leave the Soviet Union although its successes, so far, are limited This campaign is based on maximum publicity in the western press coupled with well publicized hunger strikes and demonstrations interspersed with frequent, communal, telephone calls between west and east

But how should Dr Zhores Medvedev set about regaining his lost citizenship? At first sight it would appear that a publicity campaign directed by and centred around Dr Medvedev himself would be counter-productive and would firm the resolve of the Soviet authorities to banish him Conversely no campaign at all with Dr Medvedev remaining quietly in the background, as he has done for the past seven months, hoping against hope for a change of heart and awaiting a call from the embassy, would seem to be even more hopeless

This, in essence, is the dilemma in which Dr Medvedev finds himself at present And it seems that help for him must come from the scientific community which must be prepared to act without any overt encouragement from Dr Medvedev But what is there to be done? Throwing stones through embassy windows is an exercise which after the first flush of anger and enthusiasm has worn off would seem to be futile Is this the time perhaps when invitations to Soviet scientists to attend conferences in the west should be withdrawn and participation in exchange schemes temporarily halted? Drastic measures indeed, which might damage several years of careful nurturing of Western–Soviet relations, but this is a drastic situation In the end it is only the scientific community that can decide the extremes to which it wants to go to help a colleague in distress And in this case it must not get too discouraged if there is an apparent lack of interest and cooperation from Dr Medvedev himself

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100 Years Ago

Although, as the writer observes, "in cold weather the impulse to act is much more powerfully felt than in summer, when the air is hot, and therefore the temperature of the surface is higher," yet even 98° F (the internal temperature of a healthy body) is not uncommon for the air in tropical climates, where the natives can undergo great exertions. But, according to the thermo-electric hypothesis, the nerve force must in this case be *nil*. Again, temperatures of 140° to 160° F are easily sustained for a considerable time in the Turkish Bath Under these conditions the direction of the current should be reversed , and, even supposing that positive and negative currents both acted in the same sense on the muscles and nervous ganglia, it would seem that there must be an instant of transition when the two should be balanced, and nervous force at zero, and the powers both of sensation and motion lost with it

From *Nature* **8**, 324, August 21, 1873

OLD WORLD

Medvedev still Determined to be a Soviet Citizen

DR ZHORES MEDVEDEV, in spite of the fact that he has been deprived of his Soviet citizenship, is still determined to return to live in the Soviet Union Earlier this week he said that he would appeal against the decision of the Praesidium of the Supreme Soviet made on July 16 which was based on Dr Medvedev's apparent violation of a decree passed in 1937 which allows Soviet citizens to be deprived of their citizenship if they break certain rules which apply to Soviets living abroad

In a statement issued at the end of last week, Dr Medvedev points out that it is usual for Soviet citizens who travel abroad to sign a declaration undertaking not to violate these rules and regulations But Dr Medvedev was neither shown the regulations before leaving the Soviet Union nor was he asked to sign any declaration He therefore argues that he cannot be responsible for regulations he has neither seen nor signed

Dr Medvedev's continued hope that his citizenship will be restored and his passport returned is based on a discussion he had last week with the secretary to the consular department at the Soviet embassy This gentleman told Dr Medvedev that the decision was not irreversible and that an appeal could be made through official channels But in the same conversation Dr Medvedev was informed how to obtain documents from the British Foreign Office to enable him to travel outside Britain

Dr Zhores Medvedev's difficulties with the Soviet Authorities first became evident after he attended a meeting in Paris in 1957 Soon after this, his first meeting outside the Soviet Union, he was inundated with requests to participate in meetings and research projects, and to deliver lectures abroad, but all his applications for foreign travel were turned down until late last year During these long years Dr Medvedev continued with his research work and wrote several books, the best known of which is *The Medvedev Papers*, published in 1971

Since then Dr Medvedev has had an even more difficult time with the Soviet Authorities In July 1972 he was ignominiously sent home from Obinsk by the Soviet police and refused permission to attend an International Congress of Gerontology which was being held in that city And during 1972, after receiving an official invitation from the National Institute for Medical Research to spend a year in London working at the institute's Mill Hill laboratories, his application for permission to take up this appointment was at first turned down But in December of last year, Dr Medvedev was granted a passport and he arrived in London early this year.

During the past seven months Dr. Medvedev has deliberately kept out of the limelight and he has rejected advances from the press for interviews and he also refused to take part in any political activity The one action which might have been the reason for the Soviet Praesidium depriving him of his citizenship was his signing of an agreement to publish in Britain his book, *Ten Years After Ivan Denisovich*, which was written before he came to Britain But Dr Medvedev is adamant that the book can never be used against him in the Soviet courts for it "is not political and criticizes neither the Soviet system nor the Soviet government" The book, says Dr Medvedev, "gives only a factual account of events that actually took place and cannot be considered in any way as slanderous, defamatory or anti-Soviet" This book, in fact, gives an account of how Alexander Solzhenitsyn has been treated by the authorities since he published his first novel, *A Day in the Life of Ivan Denisovich*

Dr Medvedev's twin brother Roy has issued a statement in Moscow deploring the treatment accorded his brother and he describes the deprivation of citizenship as an "absurd act" According to other reports from Moscow Dr Medvedev has lost his citizenship as a result of "actions discrediting the high title of citizen of the USSR" According to Tass, the Soviet news agency, the action by the Praesidium was taken under an article of the Soviet Legal code which deals with anti-social acts or defamation of the Soviet state Tass also added that Dr Medvedev had fabricated slanderous materials discrediting the Soviet state and social system

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NORTH SEA RESEARCH

Caught up in the Flow

ON September 10 some ninety current meters, twenty bottom mounted offshore tide gauges and three automatic buoys will be busily recording currents and tides in the southern North Sea, while more than fifty research institutes and laboratories in Belgium, the Netherlands and Britain will be waiting for the results

The operation, entitled JONSDAP 73, is intended to provide a whole host of basic data about the North Sea which can be used to produce numerical models for predicting the behaviour of one of the busiest stretches of sea in the world

JONSDAP 73 (Joint North Sea Data Acquisition Programme) is the brainchild of a body calling itself JONSIS (Joint North Sea Information Systems) which got under way in 1970 when the West German oceanographers approached the Natural Environment Research Council to suggest an exchange of information about their research in the North Sea Since then, Belgium, the Netherlands and Sweden have joined the club, and JONSDAP is the first specific project to emerge It consists chiefly of rephased programmes of the various bodies involved which have been brought together to provide one mass of data in an exercise which is planned to last at least 40 days and which will involve twenty-two research vessels.

British institutions involved include the Institute of Oceanographic Sciences, the Fishery Laboratories at Lowestoft, the Universities of Bath, East Anglia and Liverpool, the Port of London Authority and the Hydraulics Research Station Research projects on tides, storm surges, current vectors, circulation and mixing and pollution problems should all benefit from the studies.

Whereas the chief object is to provide a wealth of basic data, each country and institute has its own particular interest The Belgians and the Dutch are particularly interested in the pollution aspect of the studies—measurements of turbidity, salinity, temperature, trace metals, the release of drifters and diffusion of rhodamine dye experiments are all part of the programme—while the Institute of Oceanographic Sciences is aiming to find out more information about storm surges, particularly with a view to the development of a Thames barrier to save London from flooding

One of the more interesting parts of the study will be an attempt to monitor flow through the Straits of Dover using a cross-Channel telephone cable The technique involves sensing and interpreting the electrical signal induced by the movement of seawater through the Earth's magnetic field, and once the cable is calibrated it should be possible to continue to use it as a flow meter

If the operation is a success a large bank of data should be available by the end of 1974 And further work is planned West Germany and Sweden are not involved in this particular operation, but a similar exercise is planned for the northern North Sea in 1975

ENGINEERING

Total Technology

A LIMITED but enthusiastic backing for Total Technology emerges from a Science Research Council report published last week. Total Technology—one of those multi-disciplinary concepts that industry advocates and universities abhor—is the brainchild of Professor Hugh Ford of Imperial College London, who chaired the panel that has now recommended that PhDs in total technology should be awarded in the near future, with the intention of producing about 20 doctorates a year in the subject.

This course of action is rather more modest than the approach suggested by an earlier SRC working party on the subject chaired by Professor J. H. Horlock. His group's work laid the ground for Professor Ford's panel, but Horlock's recommendation was that at least 25% of postgraduate engineering students supported by the SRC should receive training in Total Technology by the end of the decade. In real numbers this would be about 200 PhDs a year.

But what is Total Technology? The report explains it by stating that the practice of engineering comprises research, development, design, production, marketing and operation of plant, while the service and construction industries require a special emphasis on planning and operations management. Total Technology is all these functions merged together to produce success.

What that means in practice is likely to be discovered this autumn at the Universities of Cambridge, Strathclyde and Aston where the first courses are to be run. The basic emphasis is to build up an appreciation of managerial functions combined with the ability to communicate with others during work as an engineer.

Inevitably this implies a deal of course work. But Professor Ford and his panel are adamant that they are not proposing the award of a PhD for purely course work. In the outline syllabus that is appended to their report the panel—which was drawn from industry as well as the universities—proposes that the three year doctorate should cover course work on the chief sectors of industry from raw materials to primary and secondary industry, large-scale manufacturing, mass production and small specialized industries, combined with detailed work on two background disciplines chosen from such areas as design function, industrial sociology, the economics of companies, systems analysis and plant maintenance.

This part of the course might be compressed into one year to become a master's degree, the panel suggest. But the really meaty part of the operation—the part that the panel maintain makes the operation worthy of a PhD rather than just a master's degree—is work on industrial projects. These should extend over the last two years of the course, comprising one, two or possibly three open-ended projects broadly associated with the subjects studied earlier. The choice of subject would be made in collaboration with industry. "The student would thus" the panel say, "attack an industrially relevant problem, of direct interest to the firm, and obtain a solution in a realistic time."

Clearly the panel is convinced of the value of what it recommends. But what does industry think? The reaction to Professor Horlock's original proposals was a little cool. The relevance of existing PhDs was eagerly attacked, and Total Technology as an idea was warmly received, but industry doubted whether the target of 25% of SRC-supported engineering PhDs being total technologists by the end of the decade was a desirable or even a possible target, and the old bugbear of producing more doctorates than could be employed was raised. A one year MSc was thought to be a more preferable alternative.

The result of all this is that Total Technology will appear, but slowly. The panel stresses the difficulties of introducing the subject and emphasizes that the new courses must benefit from the experience gained by their first students. A gradual introduction is more likely to produce a course that produces the type of doctorate that industry wants.

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FROM the first issue in 1974, *Nature* will appear in a single weekly edition of about the same number of pages as the present three weekly editions taken together. The single weekly edition will replace the present Friday *Nature, Nature New Biology* and *Nature Physical Science*.

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Nature has had to absorb steeply rising costs on production, paper and despatch. But, for the majority of subscribers, the new price will mean they actually pay less for *Nature* in 1974 than they are paying in 1973.

Subscribers will receive full details with their renewal notices later this year.—D. D.

Dr David Davies takes up the editorship of Nature *next Monday, August 20.*

NAUTICAL ARCHAEOLOGY

Protecting Wrecks

from a Correspondent

THE first sites of wrecks to be given protection under the recently passed Protection of Wrecks Act were announced last week by Mr Cranley Onslow, Under Secretary of State for Aerospace and Shipping. The act provides for specific wreck sites of cultural interest within British territorial waters to be given something of the status of an ancient monument on land.

British wreck sites are typically collections of related objects rather than well-preserved ancient hulls, which, paradoxically, are found in river banks, marshes and harbours. And three of the four sites initially designated by Viscount Runciman's committee will be just such a collection of historical objects.

The four sites are the royal yacht, Mary, a gift from the Dutch to Charles II and wrecked off Anglesey in 1675; the Dutch East Indiaman, Amsterdam, beached near Hastings when outward bound on her maiden voyage in 1749; Henry VIII's Mary Rose, capsized near Spithead in 1545 and preserved to her gundeck in seabed silt, and the Grace Dieu.

The Mary Rose is thought by the survey team currently working on her to be sufficiently well preserved to be raised whole. The construction of the boat is of great interest but the prospect that her contents might be recovered—the Solent silt is a good preservative—creates even more excitement. The Mary Rose is known to have sunk during a battle manoeuvre, thought to have been planned by King Henry VIII himself who watched the scene from the battlements of Southsea Castle, so the possibility is high of there being documents of great historical interest on board.

The fourth candidate, however, is a very special case. Henry V's Grace Dieu—a ship from the early 1400s—was built for wars that were over by the time she was ready. The largest ship built in Europe for over 200 years, she has lain in the tidal Hamble river since she sank. It is thought that only five feet of her timbers above the keel are left, for, in spite of being largely submerged, she has been the object of souvenir hunters for centuries and is now threatened by a motorway. Nevertheless those five feet are of compelling interest, for they are of unique triple-clinker construction.

NEW WORLD

Vitamins, Safety and Freedom of Choice

by our Washington Correspondent

In the past two years, the so-called health food industry has been going through a period of burgeoning growth in the United States. Founded on sound nutritional science and sheer quackery in varying proportions, and aided by growing public distrust of modern agricultural and food processing practices, the industry has managed to remain relatively free from government control in general and from the tiresome task of having to justify some of its more excessive advertising claims in particular. But, if the Food and Drug Administration gets its way, the health food industry is heading for a somewhat dramatic change.

Earlier this month, the FDA published a set of regulations governing the sale of vitamins and minerals and the fortification of foods which, barring successful challenge in the courts or in Congress, will force some radical changes in the promotion, packaging and sale of health foods. The regulations have, however, stirred up something of a hornets nest for they have been bitterly attacked by a variety of people and they have caused confusion and outrage. They clearly throw up some important philosophical questions.

The new regulations took ten years to draw up and are due to be enforced at the beginning of next year. In short, they will chiefly affect the sales and promotion of large doses of vitamins and minerals, but they will not greatly affect the marketing of such products in doses that the FDA reckons the average healthy person needs each day to maintain good nutrition. The key to the regulations is a switch from the Minimum Daily Requirement as the official measure of nutritional intake to a new standard called the US Recommended Daily Allowance (RDA). The old standard was simply the minimum level of each nutrient required to prevent the onset of deficiency diseases, while the RDA, which is based on criteria suggested by the National Academy of Sciences, is supposed to represent levels required for good nutrition.

The FDA has established RDAs for nineteen essential nutrients, and it is attempting to draw distinctions between ordinary foods, special dietary supplements and drugs, on the basis of the percentages of the amount of RDA they contain. In general, if a product contains less than 50% of the RDA per serving, it will be classed as a food, if it contains between 50% and 150% of the RDA, it will be classed as a dietary supplement, and those products containing more than 150% of the RDA will be classed as drugs.

Different regulations will apply to each category, but the chief effect will be that manufacturers will have to amend advertising claims, label their products appropriately, reformulate some dietary supplements to get rid of irrational combinations of vitamins and minerals and end the practice of claiming nutritional value for essentially worthless ingredients. Foods which contain less than 50% of RDAs, for example, cannot be marketed on the basis of claims of therapeutic value, while heavily fortified breakfast cereals will have to be marketed as dietary supplements rather than as foods. But as for vitamins and minerals sold in high dosages, they will eventually have to meet standards of efficacy and safety that apply to all drugs.

The idea is not, however, to force high dosage products off the markets, or even to stipulate that they should only be made available on prescription. This, in short, is what will happen. Vitamins and minerals which contain more than 150% of the RDA will, from January 1, 1974, have to be sold as drugs, bearing labels stating that they should be taken for therapeutic purposes only. With the possible exception of vitamins A and D, they will still be available in drug stores without prescription, but eventually they will all come under the general review of over-the-counter drugs which is being conducted by the FDA, and they will have to meet stringent tests of efficacy and safety. In other words, nobody will be prevented from taking large doses of Vitamin C to guard against the common cold, provided that such large doses are found to be safe and effective. (In any case, the vitamin will still be available in small dose units which could be taken by the handful.)

As for vitamins A and D, the FDA is proposing to limit high doses to prescription-only status because of their toxicity. High doses of Vitamin A taken over long periods can increase pressure within the skull and mimic a brain tumour, and they have been found to retard growth in children. Excessive doses of Vitamin D have also been shown to retard mental and physical growth in children.

Why should the FDA bother to

Education Budget

by our Washington Correspondent

President Nixon last week announced that he has nominated Dr Lowell J Paige, Dean of Physical Sciences and Professor of Mathematics at the University of California, Los Angeles, to be the new Assistant Director of the National Science Foundation for Education. The job has been vacant for nearly two years, since Dr Lloyd G Humphreys abruptly resigned in September, 1971, in protest because the Office of Management and Budget had impounded some $30 million earmarked for the NSF's education and institutional support programmes, and because he feared that even deeper cuts were on the way.

His prognosis was correct, for the foundation's budget for science education improvement sank from $73.4 million in 1972 to $47 million in 1973—again, with considerable impounding of funds by the Office of Management and Budget—and the Administration has continued its plans to phase out graduate training programmes and cut back on graduate fellowships. While the funds were being cut, however, the foundation drastically revamped its educational support programmes, concentrating on four chief areas: a scientific literacy programme, aimed at increasing the scientific education of all students, not just those intending to follow careers in science; a programme aimed at increasing the effectiveness of science teaching at all levels through support of innovative courses; a programme of research on science education to determine which elements of the programmes are successful; and the development of courses and curricula centred around problems which span several disciplines.

The cutbacks of the past two years have evoked howls of protest from the universities and from the House Committee on Science and Astronautics, which oversees the work of the NSF. But there are, however, signs of improvement, for the foundation's educational support budget is set to increase to $60 million this year, and the chances are that the upward trend will be maintained. But the most hopeful sign is that the Administration has at last decided that the NSF's education programmes are sufficiently important to require a permanent director.

regulate the health food industry, in any case? One reason is that the sale of vitamin and mineral products in the United States now runs into hundreds of millions of dollars a year, and they find their way into some 75% of US households Moreover, there is a growing tendency to fortify foods with vitamins and minerals with an accompanying blast of promotion drawing attention to the fact, Some breakfast cereals, for example, have been turned into the equivalent of high-calorie vitamin pills, and they will now have to be recognized as such The FDA thus argues that since the consumer is usually in no position to judge which formulations are based on sound nutritional science and which are inherently irrational, the door is wide open for outright deception, some protection from exploitation, unsubstantiated advertising claims and possibly harmful doses of nutrients is therefore required

But, as a flood of letters, postcards and verbal complaints has demonstrated, not everybody agrees In particular, the new regulations have met with generally favourable reactions from consumer advocates, and some nutrition scientists, but with vehement opposition from others Moreover, a bill introduced into the House of Representatives by Craig Hosmer, a Republican from California, which attempts to stop the FDA from regulating vitamins and minerals for reasons other than safety, has gathered 160 cosponsors

One person who is especially upset by the regulations is Dr Linus Pauling, the Stanford biochemist who advocated, in a best-selling book, *Vitamin C and the Common Cold*, the taking of large doses of Vitamin C to guard against colds Pauling said in a telephone interview last week that he believes the new regulations "will be to the detriment of the health of the American public", and that they are also inherently inconsistent His chief complaint is that the FDA is attempting to regulate products for which there is little or no concern over safety, and that the regulations "infringe the rights of people to decide what they want to eat"

Pauling pointed out that it is inconsistent for the FDA to regulate vitamin C and not sucrose Both occur naturally and both are sold in large amounts as purified foods, but the difference is, he said, that vitamin C is essential to life, while sucrose is not There is, however, considerable evidence of harmful effects derived from large doses of sucrose, while there is virtually no evidence of harm from large doses of vitamin C "Just because a small amount of ascorbic acid (vitamin C) is needed for life is no reason to classify it as a drug", he said . His argument is that provided there is no proof of harmful effects from taking vitamins, consumers should be free to choose what they want to eat without government interference

But not all nutritionists share Pauling's views on the matter Dr D M Hegsted, of Harvard University, for example, said last week that he "cannot, frankly, see much to disagree with" in the regulations "Somebody", he said, "should have the authority to keep the quackery at a minimum" And his views are shared by some consumer interest groups In particular Anita Johnson, an attorney with the Health Research Group, a public interest association linked with Mr Ralph Nader, pointed out that consumer advocates "have been supporting the proper testing of foods and drugs and therefore we support the idea to restrict the amounts of vitamins and minerals to levels that we know are safe" And as for the FDA itself, Dr Alexander Schmidt, the new Commissioner of Food and Drugs, pointed out, when the regulations were announced earlier this month, that the Food, Drug and Cosmetic Act of 1938 requires the FDA to insure honest and full consumer information about such products

Pauling is, however, not simply concerned about infringements of individual liberty, for he believes that the RDAs established by the FDA may be too low to ensure adequate nutrition in a proportion of the public In particular, he cited a series of experiments performed by Dr Roger J Williams of the University of Texas which indicated that inbred rats and guinea pigs differ in their requirements for nutrients by factors up to 40 He then suggested that man's requirements may similarly differ from individual to individual, and thus questioned the validity of establishing a standard which allows variation by only a factor of 3

What are the chances that the opposition to the regulations will force a change in them? One possible area for forcing a change is the Congress, but although Hosmer's bill has garnered 160 cosponsors, it was first introduced in 1967 and has never been taken up by the Commerce Committee to which it was referred Moreover, there is as yet little evidence of support for the bill in the Senate Another possibility is a legal appeal Pauling said last week that he has been talking to lawyers, exploring the possibility of a law suit against the FDA Similarly, the health foods industry can be expected to challenge the regulations in the courts But, in view of the FDA's clear mandate to ensure accurate labelling of foods and drugs, the chances that such suits will succeed is generally considered slim

One ironic footnote to the debate about vitamins and minerals is that for the past few years, the health foods industry has, in large measure, been spawned by the consumer movement The effective attacks that consumer advocates have mounted on deceptive packaging, potentially harmful additives, and lack of food value in many popular foods has caused many people to jump on the vitamin bandwaggon Now, however, the wheel has turned full circle and the health foods industry is under attack for many of the abuses that it purports to eschew

NUCLEAR SAFETY

Long Awaited Inquiry

by our Washington Correspondent

A DATE for the Joint Committee on Atomic Energy's long awaited public inquiry into the safety of nuclear reactors has at last been set The committee plans to hold three days of hearings on the matter on September 25–27, when witnesses from the Atomic Energy Commission, the Advisory Committee on Reactor Safeguards, the Atomic Safety and Licensing Board and other government agencies will present their side of the case Those hearings will be followed by another set in the autumn, when public witnesses will have a chance to air their views

First promised for late last year, the hearings have been put back several times because the Joint Committee has been waiting for the AEC to produce a report on the safety of light water cooled reactors The report, the size of a telephone directory, was finally delivered to the committee last month after having been reviewed by several groups and individuals, including some of the nuclear industry's strongest friends and harshest critics It is a candid, comprehensive account of safety questions and the commission's response to them, but the report, known as WASH-1250, also meets some of the most prominent critics head-on in a chapter added to earlier drafts The chapter includes a short discussion of emergency core cooling systems, and it also tackles some of the questions about low level radiation raised in the past few years by Professor Sternglass and Drs Gofman and Tamplin Not surprisingly, the report concludes that such critics are incorrect

The Joint Committee sessions will also explore the ramifications of recent organizational changes in the agency which took nuclear safety research out of the division of reactor development, and which ultimately led to the resignation of Mr Milton Shaw, one of the most powerful AEC officials for the pas few years (see *Nature*, **243**, 431 , 1973) It remains to be seen, however, whether the committee, which is strongly pro-nuclear, can provide the searching inquiry into reactor safety that many groups and individuals are demanding

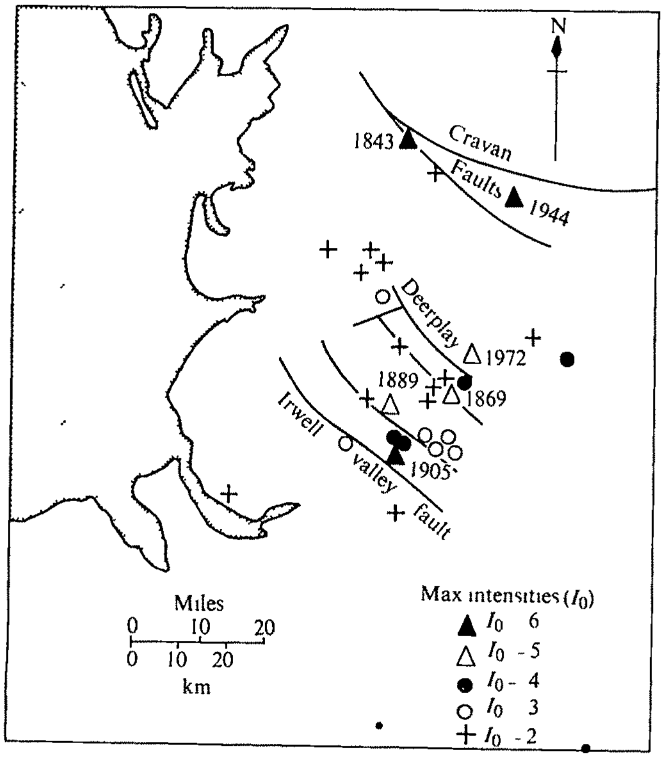
NEWS AND VIEWS

Historical Records of British Earthquakes

If asked, most people, including scientists, would almost certainly pronounce Britain to be fortunately free from the hazard of earthquakes, and if they were judging Britain by the standards of the San Andreas fault, the Japanese trench and other sections of the system of worldwide earthquake belts so elegantly defined by recent observation and plate tectonics they would have expressed a reasonable opinion But they would not be literally correct, for not only is Britain earthquake-prone, earthquakes occur quite frequently The late Charles Davison listed no less than 1,191 genuine earthquakes from the year AD 974 when, according to Symeon of Durham "a great earthquake took place over all England", to January 26, 1924, when Hereford was afflicted by an earthquake for the twentieth time in 70 years

Of course, most of these events were relatively small, but quite a number reached intensity VIII on the Rossi–Forel scale (VII–VIII on the Modified Mercalli scale) and one even reached intensity IX ("chimneys thrown down and cracks made in the walls of about one-half the houses in one place" according to Davison's simplified form of the Rossi–Forel scale) In other words, though Californians, Japanese and Sicilians might be entitled to laugh at the idea of British earthquakes, there can be no doubt that many British cities are susceptible to an unpleasant amount of earthquake damage

One of the interesting, though not unexpected, features of Davison's list of historic earthquakes is that both the number of events and the proportion of smaller shocks appear to increase significantly with time However, this is much more likely to reflect the gradually improving reporting efficiency of an increasing and increasingly educated population than any fundamental change in Britain's seismic characteristics Only ninety-eight earthquakes were recorded up to the middle of the eighteenth century, and most were reported only very briefly by contemporary or later chroniclers with many other things on their minds Thus, for example, did Holinshed record that "on the mondaie in the weeke before Easter [1185], chanced a sore earthquake through all parts of this land, such a one as the like had not beene heard of in England sithens the beginning of the world For stones that laie couched fast in the earth, were remooued out of their places, stone houses were overthrowne, and the great church of Lincolne was rent from the top downwards" From this sort of evidence Davison was sometimes able to assign an approximate intensity (VIII in this case), although it is clear that only the larger of the British earthquakes would ever have been noticed in the first place



Location of past events and major faults in the Lancashire region

But in 1750 something occurred which could hardly go unnoticed in the increasingly scientific climate of the times and which was to lead to the first serious scientific study of British earthquakes For in that year, the "year of earthquakes" as William Stukeley called it, no less than four earthquakes of intensity VII took place—two in London, one in Chichester and one in Northampton One result was that between February 19, when the first London event occurred, and the end of the year about fifty papers on the subject of the 1750 earthquakes were presented before the Royal Society, not to mention several other more general papers inspired by the same events More importantly perhaps, the interest aroused by the year of earthquakes induced scientists to begin making lists of both British and foreign shocks and thus to pay more attention to earthquake reporting

The recording of British earthquakes during about the following two centuries left much to be desired, of course, because neither the physical nor mathematical apparatus was adequate for what one would now regard as essential description The concept of magnitude, for example, was not invented until the 1930s and instrumentation, though improving all the time, has only recently achieved anything like a respectable coverage (Some would dispute even that.) Nevertheless, the largely non-instrumental techniques using arbitrary (intensity) scales of measurement did allow scientists to construct fairly complete pictures of what are now termed the macroseismic aspects of Britain's larger earthquakes

The largest intensity (IX) earthquake known in Britain occurred on April 22, 1884, in Colchester and did much to disabuse the Victorians of the idea that British earthquakes are all harmless curiosities The damage was so great, in fact, that a disaster fund (the first?) was set up to help those owners of the 1,213 buildings needing repair who were unable to bear their own costs But although the Colchester shock exceeded all others in terms of concentrated severity, the number of towns and villages damaged, the area of structural damage and the total disturbed area were far greater in the Hereford earthquake of December 17, 1896 (intensity VIII) Moreover, the residents of Hereford would have had cause to consider themselves unjustly treated, for an event of the same intensity had occurred there only 33 years before. It is certainly a pity that these and many other events were too early to have magnitudes determined because intensity involves so many factors other than seismic energy. Of British earthquakes recorded since magnitude scales were introduced, the strongest (m_b=4.9) occurred in the north of England near Kirkby Stephen on August 9, 1970 (see Browning and Jacob, *Nature*, **228**, 835, 1970).

The Todmorden earthquake of March 7, 1972, details of which are reported by Lilwall and Riddle in next Monday's *Nature Physical Science* (August 20), was far from being the largest British earthquake, either in magnitude (4.0) or intensity. But what it does share, with other larger and smaller British events is its obscure origin. Very little, if any, detailed work has ever been done on the causes of earthquakes in Britain, but since no plate boundary passes anywhere near the country it may safely be assumed that relatively minor fault slippage is responsible, even though epicentres very often fail to correlate with surface faulting. Little direct evidence is available, but as the accompanying map shows for the Lancashire region, epicentres of the Todmorden and other nearby historic events are clearly related geographically to the faulting in the local Carboniferous rocks. P J S

PROTEINS

Finger on the Pulse

from our Molecular Biology Correspondent

WHETHER the protagonists in this tale of the true nature of protein structure were conscious of the benign shade of Linderstrøm-Lang at their elbow is not recorded in their papers, but it is remarkable how closely the results and even the tools with which they were quarried were prefigured in his work of twenty years ago and more. Now that the ground rules of structure, as seen in static terms, have been laid by the crystallographers, and the thermodynamic basis of conformational stability is in principle established, it is now the dynamic characteristics of globular proteins over which the moving finger is increasingly hovering. The work of Anfinsen and his colleagues, on the interaction of peptide fragments of staphylococcal nuclease to make enzymatically active species, which has already produced so many diverting lessons in protein chemistry, has also now made possible a pretty demonstration of structural fluctuation, or breathing, in the native conformation.

The nuclease consists of a chain of 149 residues, of which the first five are dispensable, and the remainder can be non-covalently reconstituted by mixing the fragments derived by cleavage at residue 49. The complex has all the conformational and enzymatic characteristics of the pristine nuclease. Taniuchi (*J biol Chem*, **248**, 5164, 1973) has now made such a modified enzyme by mixing the fragment (6–48) with preparations of (50–149), labelled with radioactive acetyl groups at three places in the chain. When this complex was mixed with unlabelled (50–149), it was possible to observe exchange of the latter with its labelled counterpart in the native conformation, a reaction that can occur only by dint of transient unfolding to break the numerous non-covalent interactions that stabilize the association of the two parts of the chain. Fragment and enzyme are easily separated by affinity chromatography on a column bearing the bound inhibitor, thymidine diphosphate, and with this system exchange of partners can be detected within minutes. There is a strong temperature effect, but even at 4° C the exchange looks to be heading for completion after a few hours. At 15° C, the rate follows a first-order law, though at 4° C there is some deviation at longer times. The activation energy is large,

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Ribosomal Genes in Higher Organisms

GENETIC studies on microorganisms have the great advantage that the doubling time is relatively short and this facilitates the production of large masses of selected mutant strains. Mapping genes for ribosomal RNAs and ribosomal proteins, for example, is much more straightforward in *Escherichia coli* than it is at present in the case of higher organisms. Still, some progress may be reported in the case of the fruit fly *Drosophila* on which genetic studies have been carried out since early in this century. The bobbed (bb) bristle phenotype is known to be associated with reduced ribosome synthesis and in *Nature New Biology* next Wednesday (August) 22) Steffensen examines the ribosomal proteins of variants of the bobbed phenotype by polyacrylamide gel electrophoresis (unfortunately in only one dimension). He was unable to detect any difference, but his findings do not exclude the possibility that there are differences which might be discovered by using fractionation methods affording higher resolution of the ribosomal proteins. Screening of ribosomal proteins from 80S *D melanogaster* particles of adult XY males or XO males and XX or XXY also failed to turn up any differences by the same criterion. There were, however, several differences between the ribosomal proteins of *D melanogaster* and *D simulans* and their hybrids. Steffensen describes the optimal conditions for producing 60S and 40S subparticles of ribosomes from these species and correlates changes in the electrophoretic patterns of the ribosomal proteins with the genetic constitution.

Steffensen locates seven variants of ribosomal protein genes, three from the 40S, and four from the 60S subunit, in the X chromosome near, and to the left of, the nucleolus organizer. More precisely, it seems that the genes corresponding to the variant proteins may lie in the block between *ot* (outstretched) and *unc* (uncoordinated) which includes section 19A-E or about twenty-six bands on the map of the salivary X chromosome. Preliminary evidence leads Steffensen further to suspect that segment 19E may be responsible for the variant proteins. The proximity of the ribosomal protein genes to the nucleolus organizer is interesting because the nucleolus organizer contains the DNA which codes for ribosomal RNA. Steffensen predicts that the genes for all the ribosomal proteins in *Drosophila* will be found clustered in the same region near to that of rDNA as indeed has been found to be the case in *E coli*.

Timmis and Ingle in this same issue of *Nature New Biology* have studied the levels of rDNA in descendants of the plastic genotroph (P1) of flax which produces a large stable form (*L*) or a small stable form (*S*), according to the fertilizers applied. The *L* genotroph contains 16% more DNA than that of *S*, with P1 intermediate. Cytological observations moreover indicate that the nucleolar dry mass in the *L* form is twice as great as that of the *S* form. Comparisons are made with the Mexican axolotl and *bobbed* mutants of *Drosophila* in which the size of the nucleoli has been directly correlated with the redundancy of rDNA.

Hybridization experiments by Timmis and Ingle confirm their hypothesis that the same type of differences may occur in these examples from the Plant Kingdom. Indeed they find that the percentage hybridization of the *S* DNA was 0.34 and 0.53 with the large and small subunit ribosomal RNAs, respectively, whereas the corresponding figures for the *L* DNA were 0.52 and 0.76, respectively—roughly 70% greater. The total number of genes was calculated in each case: in *S* DNA, 2,095 and 2,055 for the large and small subunit ribosomal RNAs respectively, in *L* DNA, 3,315 and 3,534, for the corresponding RNAs.

and of the order associated with denaturation of proteins. Moreover the rate varies in first-order fashion with the concentration of the complex, and is independent of that of the free fragment, which indicates that the process is limited, as one would suppose, by the unfolding, or breathing frequency, rather than the reassociation rate, which is known from earlier studies to be fast. Now although the stability of the complex is somewhat lower than that of the integral enzyme, as judged by the thermal denaturation temperature, it may reasonably be inferred that the breathing equilibrium obtains in the latter. The cooperativity of the conformational equilibrium ensures that the native state will normally be overwhelmingly populated. Addition of the inhibitor, TDP and calcium ions, causes a dramatic reduction in the exchange rate by stabilizing the native structure.

The dynamic state of the native conformation, and the transient appearance of an unfolded form, is equally reflected in the kinetics of hydrogen exchange, an approach conceived long ago by Linderstrøm-Lang. The internal exchangeable hydrogens in a globular protein evidently become available by this mechanism, and Takesada, Nakanishi and Tsuboi (*J. mol. Biol.*, 77, 605, 1973) have now extended their earlier analysis, based on the use of infrared spectroscopy to follow the exchange of peptide hydrogens against deuterium, to another protein, α lactalbumin. The supposition is that the unperturbed exchange rate for accessible protons is attenuated by a factor representing the equilibrium concentration of the unfolded form. Now the thermal denaturation profile can be used to yield the enthalpy and entropy of unfolding, and thence to derive the conformational equilibrium constant at temperatures outside the transition range, where the denatured state cannot be detected by spectroscopic methods. For lysozyme this constant leads to an excellent quantitative fit of the hydrogen exchange kinetics. There was also, as in staphylococcal nuclease, a large stabilization of the native state when specific inhibitors were introduced. In α lactalbumin there is a difference between the equilibrium constant for unfolding within the optical transition, and that inferred from hydrogen exchange at lower temperatures, which is most easily explained in terms of the existence of locally unfolded intermediates which govern the exchange rate. The number of slowly exchanging peptide hydrogens is thirty-five in lactalbumin, compared with forty-four in lysozyme, and this difference can be rationalized in terms of differences in the number of inferred intrapeptide hydrogen bonds in the conjectural lactalbumin structure, derived by fitting the sequence to the X-ray model of lysozyme, to which it is closely related.

Local structural fluctuations also explain new tritium-exchange results of remarkable refinement, obtained by Englander and Rolfe (*J. biol. Chem.*, **248**, 4852, 1973) on liganded and unliganded haemoglobin. This work represents the next stage of evolution of the method, for Englander has found that any transfer of exchangeable protons from a slower to a faster exchanging category, in consequence of a conformational perturbation of the protein, can be observed with great precision after partial tritiation of the protein in one of its two states, by measuring the exchange-out rates, first when it is in the same state, and then when it is in the other. By manipulating these combinations of exchange conditions, it is possible to obtain difference curves for exchange in the two states. Moreover, by choosing the time range (just as in relaxation experiments), from seconds to days, one can home in at will on the group of protons that show the most interesting differences. In haemoglobin, Englander and Rolfe find that there are three groups of protons, three, eight and nine in number, the exchange of which is ligand-sensitive. All of them exchange much faster in the liganded protein. Inasmuch as the rates are, as before, limited by the equilibrium between folded and (in this case locally) unfolded chain segments, an equilibrium constant and free energy can be attached to the conformational element corresponding to each group. A small energetic change, involving perhaps 2 kcal/mole, is sufficient to give rise to a readily measurable effect on the exchange, such as here observed. The greater local stability of the deoxyhaemoglobin befits what is regarded as the "relaxed" state, the haem ligand perturbing the conformation in the direc-

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Immunoglobulin mRNA Sequences

The exploratory work on messenger RNA sequences was for practical reasons confined to viral RNAs of *Escherichia coli*. The consequent development of highly sophisticated sequencing methods evolved to cope with the problems which arose in this work has opened up the possibility in future of sequencing other nucleic acids. The next obvious stage is to compare the sequences of these viral messengers (which are likely to possess distinctive functional sequences, for example, for replicative purposes) with those of normal cellular messengers, and to compare the sequences of eukaryotic and prokaryotic mRNAs, of both cellular and viral origin. Brownlee *et al.* (see *Nature New Biology* next Wednesday) have made an important step in this direction by determining the sequences of five long stretches within the mRNA chains for mouse immunoglobulin light chains from a myeloma tumour cell line grown in tissue culture.

The advantage of this system over many others from eukaryotes is the possibility of obtaining pure mRNA sufficiently highly labelled with ^{32}P for sequencing operations. Despite lack of mRNA contamination of the relevant 12–14S RNA fraction isolated by sucrose gradient centrifugation, there proved to be contamination with mitochondrial ribosomal RNA in the same size range. Brownlee *et al.* overcame this difficulty by using oligo(dT)cellulose column chromatography, the messenger being more tightly bound by virtue of its poly (A) "tail". Four out of five long sequences (more than eighteen residues) in the purified messenger were found to correspond, with reference to the genetic code, to known amino acid sequences in the corresponding mouse immunoglobulin light chains. Moreover, the authors were able to deduce from their results the actual triplet codons (where several might be possible owing to the degeneracy of the genetic code) which have been selected for specific amino acids in the immunoglobulin sequence. The nucleotide sequence of a fifth long fragment of the messenger does not correspond to any known amino acid sequence in the light chains and therefore is presumed to be located outside the coding region of the RNA.

The molecular weights of the immunoglobulin light chain mRNA and its 3′-poly (A) "tail", isolated after digestion of the intact mRNA with nucleases, were determined from the electrophoretic mobilities of these species in polyacrylamide gels containing formamide. It is concluded that the total length of the molecule is 1,200 residues and that of the poly (A) "tail" is 200 residues. By comparison, the poly (A) "tails" of HeLa cell mRNA are also about 200 residues long, but those of the mouse globin mRNAs are only 40–80, and that of polio viral RNA is only about 90, histone mRNAs contain none. The coding region must be 690 residues long (3 times the number of amino acids). Subtracting this number plus 200 residues of the poly (A) "tail" from the total length of the molecule leaves 300 extra bases. It is not yet known how these are distributed between the 3′ and 5′ ends of the mRNA, but it is interesting to note that the 5′ terminus of the sequenced viral RNAs (MS2 and R17) and rabbit globin mRNA contains only about 150 extra bases at the 5′ end.

tion of higher conformational energy Reasonable conjectures can then be made from Perutz's structural data about the segments associated with the responsive groups of protons The method clearly has great potential for wider exploitation, based as it is on the amplification of energetically minuscule events

DNA SYNTHESIS

Filling the Gaps

from our Molecular Genetics Correspondent

THE idea first proposed by Okazaki that DNA chains are synthesized in short pieces which are only later joined together explains many of the problems of replications, in particular how two chains of opposite polarity are synthesized by an enzyme which moves in only one direction But no DNA polymerase yet discovered is able, *in vitro* at any rate, to start synthesis of a chain A solution to the problem of how each Okazaki fragment is started was first proposed by Okazaki and his colleagues last year and is now expanded in more detail by Hirose, Okazaki and Tamanoi (*J molec Biol*, **77**, 501, 1973)

Each fragment of DNA starts off with a length of RNA according to this model, the RNA is removed before synthesis of the fragment is completed The RNA–DNA nascent fragments can be isolated by their buoyant density, greater than that of single strands of DNA, in CsCl gradients The proportion of RNA can be estimated from the extent of the buoyant density shift and Hirose *et al* report that pulse-labelled Okazaki fragments of 400–2,000 nucleotides contain an RNA segment of 50–100 nucleotides The same length is estimated by measuring the decrease in the length of the fragments when the RNA moiety is degraded by alkali or RNase, and RNA chains of this length can be isolated after degradation of the DNA moiety with DNase

If the RNA chain initiates each fragment, it must be located at the 5′ end The small shift in size of the fragment when RNA is removed shows that it must be located at one end, labelling the 5′ base by removing its phosphate and replacing it with ^{32}P confirms that it is part of RNA After the RNA has been degraded, similar experiments can be used to label the first base of the remaining DNA chain The number of 5′ RNA and DNA termini labelled in this way is always identical, confirming that one RNA sequence lies at the beginning of each DNA fragment The first base of the DNA chain is always cytidine and the last base of the RNA is always a pyrimidine, so that it is possible that a specific sequence—presumably repeated very many times in the *Escherichia coli* genome—provides the point of switch from RNA to DNA The ineluctable progress of Okazaki's research therefore makes inescapable the conclusion that DNA chains must start with RNA, leaving for resolution the important questions of the sequences (if any) which dictate where RNA synthesis begins and ends and the nature of the RNA polymerase which transcribes them

While or after the RNA is removed by an unknown mechanism, the 3′ end of one Okazaki fragment must be extended to the 5′ end of the next fragment But this leaves a break in the integrity of the phosphodiester chain between the two fragments The existence and making good of this nick has been one of the more controversial aspects of the Okazaki model for discontinuous growth of DNA chains The enzyme polynucleotide ligase has been implicated in this action during phage T4 replication, but mutations in the ligase of *E coli* have produced more equivocal results, taken to cast some doubt on the idea that ligase has this function in bacterial replication

Mutations in the ligase gene of *E coli* have now been placed in a standard genetic background by Gottesman, Hicks and Gellert (*ibid*, 531) and Konrad, Modrich and Lehman (*ibid*, 519) One ligase mutant, *lig-4*, was originally isolated as a double mutant, *lig-4 lop-8* The *lig* mutation produces a ligase enzyme defective at high temperature, *lop* increases the amount of enzyme in the cell without altering its sequence and is therefore a control mutation of some kind Both map close together Another ligase mutant, *lig ts-7*, was isolated in a genetic background containing many other mutations and has now been separated from them, *lig-4* has been separated from *lop-8*, so that two strains of ligase mutant are available for analysis

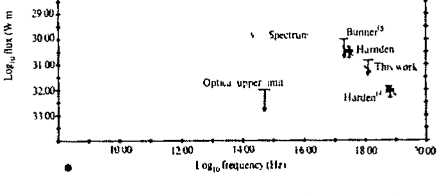
Both strains have at high temperature a much impaired ability to join together Okazaki fragments and therefore accumulate 10S pieces of DNA Although the *lig ts-7* mutant is a conditional lethal which dies at high temperature, the *lig-4* mutant can grow in these conditions The cells of *lig ts-7* are less active in ligase function at high temperature than those of *lig-4*, so that the continued viability of the latter mutant may be due to the persistence of some ligase activity even at high temperature

Ligase is clearly identified by these experiments as the enzyme responsible for the final step in joining together the Okazaki fragments Because double mutants of *polA* and *lig-4* are inviable at high temperature, it is possible that the Kornberg polymerase I may also be involved in this step and perhaps in the removal of RNA and extension of Okazaki fragments until they are adjacent The *lig-4* cells have only 1% of the wild type ligase activity at high temperature, *lig-4 lop-8* double mutants have about 5% Both cell types can grow, although defective in sealing Okazaki fragments together, this points to the conclusion that cells contain far more ligase activity than they need, explaining the reason for mutations producing equivocal results when higher levels of ligase activity are possible It is necessary to achieve a very great reduction in the ligase activity to prevent its action in replication The purpose of the excess ligase activity is a matter for speculation at present, but it may be implicated in repair and recombination pathways

X-Ray Flux from the Vela Pulsar

IN next Monday's *Nature Physical Science* (August 20) Cruise and Newton report X-ray observations of the vicinity of PSR0833-45 (the Vela pulsar) and two other pulsars Because there is a strong dependence of pulsar luminosity on pulsar period, it is not surprising that no X rays were detected from MP0833-40 (period 0 766 s) or from MP0736-40 (period 0 375 s), but they were observed because of their proximity on the sky to the Vela pulsar (period 0 089 s) The observations of the latter, however, help to provide constraints on the nature of the pulsar's spectrum (see figure)

The observations were made using a proportional counter sensitive in the range 2 8 to 9 9 keV, mounted on a Skylark rocket flown from Woomera on November 11, 1970 Together with two positive observations by Harnden (*Astrophys J Lett*, **172**, L91, 1972) and upper limits due to Bunner (*Goddard Space Flight Center Report* X-683-71-375), the latest upper limits require that the spectrum is either a power law with exponent −1 or an unusual spectrum with a double peak in the X-ray region A power law spectrum of injected electron energies, with exponent −2, would produce the required X-ray spectrum, according to Cruise and Newton



Pulsed energy spectrum of the Vela pulsar, PSR0833-45

LIQUID HELIUM

Nuclear Cooling

from our Condensed Matter Correspondent

THERMAL contact between a metal and liquid ^{3}He at temperatures of a few mK can be greatly enhanced by adding a small proportion of magnetic impurities to the metal, This important experimental effect has been demonstrated by Avenel, Berglund, Gylling, Phillips and Vetleseter of the Helsinki University of Technology, working in collaboration with Vuorio of the University of Helsinki (*Phys Rev Lett*, **31**, 76 , 1973)

Temperatures significantly below 1 mK have been reached only through adiabatic nuclear demagnetization, by which the system of nuclei in, for example, a piece of copper can be cooled to a few μK Unfortunately, however, this technique has been of little practical use, chiefly because of the difficulty of making satisfactory thermal contact at these temperatures The need, engendered by the recent discovery of new, perhaps superfluid, phases of ^{3}He, to carry detailed investigations of the liquid to well below 1 mK will probably be met, eventually, only through use of nuclear cooling, so it has become a matter of prime importance that a method should be devised for achieving adequate thermal contact between metal and liquid at these temperatures

When heat, in the form of a net flow of phonons (quantized lattice vibrations, travelling at the velocity of sound), passes across a boundary between two different materials, there is always a discontinuity in temperature across the interface as a result of the so-called Kapitza boundary resistance, R_B This phenomenon, which arises from the different velocities of sound in the two materials, becomes very much more marked as the temperature is reduced (in fact $R_B \propto T^{-3}$), and the discontinuity takes a particularly large value in the case of a helium to metal interface simply because the acoustical velocity mismatch is then especially severe For this reason, it usually takes an exceedingly long time to establish thermal equilibrium between liquid ^{3}He and a solid with which it is in thermal contact

Abel, Anderson, Black and Wheatley, then of the University of Illinois, were therefore surprised to observe that thermal contact between liquid ^{3}He and the paramagnetic salt cerium magnesium nitrate (CMN) was anomalously good (*Phys Rev Lett*, **16**, 273 , 1966) They found, in fact, that the thermal equilibrium time for a mixture of powdered CMN and ^{3}He was only a few tens of seconds, considerably less than the time predicted from a value of R_B calculated on the basis of phonon conduction Furthermore, the measured R_B varied as T^{-1} rather than T^{-3}, which suggested that heat was being transferred across the interface by an entirely different mechanism

Leggett of the University of Sussex and Vuorio were later able to explain this phenomenon in terms of a direct interaction between the magnetic moments of the ^{3}He nuclei and the electronic spin magnetic moments of the cerium ions in the CMN (*J low temp Phys*, **3**, 359 , 1970) Their proposal was that most of the heat is carried across the interface, not in the form of phonons, but as a result of the electronic spin system in the CMN being able to "talk" directly to the nuclear spin system of the ^{3}He, and they were able to show that this process would result in a T^{-1} dependence of R_B, as observed It was suggested, therefore, that, by a similar mechanism, R_B between ^{3}He and a metal might be reduced if the metal were "doped" with a small proportion of magnetic ions, which could then communicate directly with the ^{3}He nuclei The experiment now reported by the Helsinki group shows unambiguously that this is so

In one experiment, a thin palladium foil of area 254 cm^2 and containing 32 p p m of iron was immersed in liquid ^{3}He The foil was welded to a piece of high purity copper whose temperature, and thus that of the foil itself, could be derived from measurement of its nuclear magnetic susceptibility The temperature of the ^{3}He was determined by measuring the magnetic susceptibility of powdered CMN immersed in it Heat was supplied at a constant rate, and the temperature difference between the foil and the ^{3}He was carefully monitored as the whole assembly gradually warmed up R_B was found to vary as T^{-1}, just as for an interface with CMN, and at 4 mK was fifty times smaller than would have been expected for a pure palladium foil, assuming conduction only by phonons

Although R_B will need to be reduced by an even larger factor before nuclear demagnetization can become a really useful tool for cooling liquid ^{3}He, the results of the Helsinki experiment are distinctly encouraging ●

Subduction Beneath Barbados

ALTHOUGH most of the Atlantic continental margins are not plate boundaries, there are a few border areas where oceanic lithosphere is thought to be descending One of these lies in the vicinity of the Lesser Antilles island arc where, although crustal structure is known in very general terms, the precise position and nature of the subduction zone have remained unclear In next Monday's *Nature Physical Science* (August 20), however, Westbrook *et al* report the results of a geophysical survey which has enabled them to present a more detailed model of the nature and behaviour of the descending crust near Barbados

The principal data come from an east–west seismic refraction line to the east of Barbados, and show that the Moho dips by 1 3° or 2 0° towards the island (assuming velocities of 8 1 or 8 3 km s^{-1}, respectively, beneath the Moho) and that the oceanic layer dips in the same direction by about 1° What these results mean is that over 50 km away from, and to the east of, Barbados, at least, there is no significant descent of the oceanic lithosphere But an interpretation involving a combination of the seismic data, gravity observations and other seismic results from the west of Barbados shows that closer in towards the island the oceanic crust begins to dip much more steeply from both the east and west At the same time the sediment gets thicker from both directions until beneath Barbados itself it reaches a maximum thickness of about 18 km

Thus although there is a long gentle slope downwards from the east in the oceanic lithosphere, the subduction zone proper only begins beneath Barbados itself—and this is confirmed by the lack of earthquake activity to the east of the island Moreover, the sedimentary thickening towards a maximum indicates a sediment-filled trench structure, also beneath the island Reflexion experiments show that the sediments themselves are deformed, both in the trench structure and over the relatively flat lying oceanic crust to the east Westbrook and his colleagues attribute this deformation to the piling up of sediment as the Atlantic ocean floor moves westwards beneath Most of this piling up occurs to the east of Barbados, although the reflexion data also suggest that some sediment is being thrust over the plate to the west of the Barbados Ridge

Finally, assuming that the natural thickness of the sediment accumulating on the westward-moving oceanic crust has remained roughly constant over the estimated 60 million-year age of the Lesser Antilles, the volume of sediment now in the Barbados pile would imply an average subduction rate of 1 0 cm yr^{-1} This compares with a figure of 0 52 cm yr^{-1} derived from the fact that the leading edge of the descending lithosphere, assumed to be represented by the lower limit of earthquake foci, has apparently reached a depth of 200 km during the same 60 million years

COMPACT OBJECTS

Still More Questions than Answers

from a Correspondent

ONE current focus of astronomical interest concerns the existence and properties of compact objects where matter is compressed to an exotic high density state, and where gravity may be so strong that relativistic effects are crucially important This was the theme of a three-week international meeting on the physics and astrophysics of compact objects held at the Cambridge Institute of Astronomy on July 2–20 and sponsored by the NATO Scientific Affairs Division

It was of course the discovery of pulsars in 1967 which provided the first strong evidence that neutron stars actually occur in nature An intensive recent search by astronomers at Jodrell Bank has boosted the number of known pulsars to 100, and the present data were summarized by Professor F G Smith Several theorists—including Professor F D Kahn and Dr L Mestel (University of Manchester), Drs F C Michel (Rice University) and R N Henriksen (University of Sussex)—discussed the magnetospheres of spinning neutron stars The complexity of this subject even in the case when the magnetic and rotation axes are aligned, suggests that it will still be some time before the non-axisymmetric problem—a prerequisite for any real understanding of the origin of the radio pulses themselves—is properly solved. Precise timing data on pulsar periods and their derivatives can in principle tell something about the nature of the electromagnetic torques whereby the rotational kinetic energy is transformed into pulsed radiation and fast particles The pulsar NP0531 in the Crab Nebula, with the shortest known period, is the most interesting in this respect Dr E Groth (Princeton University) presented data suggesting that these torques depend on the 3 5th power of the spin rate Random jitter superposed on this secular trend is attributed to "micro-starquakes" which cause fluctuations in the moment of inertia of the neutron star

Within the past two years the Uhuru satellite has revealed a class of X-ray sources which in some ways resemble pulsars For instance, the X rays from Hercules X-1 pulse with a regular repetition rate of 1 24 s This source is a member of a binary system, and orbits around its companion every 1 7 d The latest data on these sources were presented at the meeting by Dr H Gursky (American Science and Engineering) The consensus among theorists is that Hercules X-1 resembles a pulsar in the sense that rotation of a neutron star provides the "clock" It differs from a pulsar, however, in that the power radiated comes not from rotational kinetic energy but from the gravitational energy of material accreted from the companion star The infalling material is funnelled down the magnetic field lines and impacts on the neutron star surface at ~0 3c The kinetic energy liberated heats the magnetic polar caps to temperatures of several keV, so that thermal X rays are emitted

Detailed models based on this general scheme were presented by Dr F Lamb (University of Illinois) and by several other participants The long-term behaviour of Hercules X-1 is very puzzling In particular, the apparent 35-d period (in which the X rays seem to be completely extinguished for ~22 days out of every 35) stimulated several interpretations Some of these involved the idea that there is some kind of "negative feedback" whereby the pressure of the X-radiation stems the accretion flow , another possibility is that a free precession of the neutron star (analogous to the Earth's Chandler wobble) is involved The latter suggestion would be tenable only if the cores of neutron stars could be rigid solids The possibility that nuclear matter may crystallize at densities $\gtrsim 10^{15}$ g cm^{-3} was discussed by Drs C Pethick and J Shaham (University of Illinois) and by Dr S M Chitre (NASA) The issue is still controversial, but is important not only for Hercules X-1 but also for the theory of starquakes and "glitches" in pulsars

The X-ray source Cygnus X-1, which also lies in a binary system, differs from Hercules X-1 in that the X-ray emission flickers rapidly but irregularly It is widely conjectured that in this system the compact object is not a neutron star but a black hole, and that the X rays come from hot gas swirling down into the hole Alternative models for Cygnus X-1 cannot yet be ruled out (though some would be excluded if it could be definitely established that the mass exceeded the theoretical upper limit for either neutron stars or white dwarfs) Nevertheless the possibility that some of the most crucial predictions of Einstein's theory may soon be subject to observational test was sufficiently exciting to guarantee a strong representation of general relativists at the meeting The key property of black holes, according to general relativity, is that once they have formed they quickly settle down to a stationary state essentially characterized by only two parameters mass and angular momentum Thus the "Kerr solution", once regarded as a special and perhaps atypical case, is now believed to be of paramount importance because it describes the metric around any black hole The theorems establishing this result, due to Israel, Carter, Hawking and others, involve high-brow mathematical techniques Speakers at the meeting, in particular Drs J Bardeen (Yale University) and K Thorne (Caltech), addressed themselves primarily, however, to more straightforward questions pertaining to the flow of material in the vicinity of black holes and the characteristics of the emitted radiation Conceivably the radiation from Cygnus X-1 or some similar source will reveal some pattern which will enable one to diagnose the precise form of the metric Until this can be done (and at the moment it seems a remote possibility) the existence of these objects certainly cannot be adduced as evidence for general relativity, since most other theories of gravity also predict black holes (in the sense of objects surrounded by a "horizon", out of which no signal can be transmitted)

Quite apart from their obvious importance to specialists in relativity and the physics of dense matter, the existence of neutron stars and black holes poses the question of how they formed Drs W D Arnett (University of Texas) and J C Wheeler (Harvard University) discussed the late stages of stellar evolution and supernova explosions At present it is uncertain which type of explosion will leave a neutron star and which will leave a black hole Some supernovae may even disrupt the original star completely, leaving no compact remnant at all The formation of compact objects in close binary systems is harder to analyse, because of the likelihood that material will be transferred from one component to the other or else lost from the system in the course of the evolution Why, also, did the supernova explosion not disrupt the binary system? Possible scenarios were presented by Dr E van den Heuvel (University of Utrecht) Drs J Faulkner (University of California, Santa Cruz) and G Bath (University of Oxford) discussed the relation of these X-ray sources to other puzzling phenomena involving close binaries, such as novae and cataclysmic variables

As was emphasized by Dr S I Shapiro (Princeton University) isolated stellar mass black holes are much less readily detectable than those in binary systems, because inflow of interstellar matter would render them only very faint emitters Black holes of much larger mass in intergalactic space would, however, accrete at a much higher rate and could, according to Dr J E Pringle (University of Sussex), perhaps be detected Dr J E Gunn (Caltech) pointed out that such objects would in any case reveal themselves by way of the gravitational lens effect if they were sufficiently numerous

Many theorists have speculated that the phenomena associated with active galactic nuclei and quasars may involve a scaled-up version of the same processes as occur in pulsars and compact X-ray sources Specific ideas along these lines were presented by Drs J P Ostriker (Princeton University) and R D Blandford (University of Cambridge) But data on these faint extragalactic objects accumulate relatively slowly although remarkably detailed new spectra of some high redshift quasars were reported by Dr P A Strittmatter (University of Arizona) There seems much less chance of achieving any real understanding of these extragalactic objects in the near future than in the case of pulsars and X-ray binaries At the meeting Professor G Burbidge (University of California, San Diego) reiterated his doubts about whether the quasars are at cosmological distances, and one suspects that this level of basic scepticism may be just as legitimate in five years' time as it is now

It was perhaps not surprising that this meeting raised more questions than it answered The nature of these questions is such that their solution demands the collective expertise of physicists and astronomers with a broad range of skills They also require data, or even coordinated observations, spanning the whole accessible electromagnetic spectrum Studies of these enigmatic compact objects have thus already helped both to stimulate collaboration between astronomers using different observational techniques, and to incorporate astrophysics and relativity more fully in the mainstream of contemporary physics

NUCLEAR PHYSICS

Potential Ambiguities

from our Nuclear Structure Correspondent

SEVERAL recent investigations have shown that the ambiguities in the optical potentials describing the elastic scattering of helions and alpha particles by nuclei disappear at high enough energies, usually above about 100 MeV A semi-classical analysis by Goldberg and Smith (*Phys Rev Lett*, **29**, 500 , 1972) showed that this can be understood in terms of the maximum (or critical) scattering angle θ_c The ambiguity is only resolved if the differential cross-section is known for angles greater than θ_c The critical angle decreases as the energy increases, so that it only becomes possible to resolve the ambiguity above a critical energy, provided the cross-section is measured to large enough angles The critical angle also increases with the nuclear mass, A, so that it requires a higher energy to resolve the ambiguity for heavy nuclei than it does for light nuclei (see *Nature phys Sci*, **239**, 66 , 1972)

Further insight into this question has now been obtained by the quantum-mechanical analysis of Goldberg, Smith, Pugh, Roos and Wall (*Phys Rev*, **C7**, 1938 , 1973) They examine the behaviour of the phase shifts for each partial wave as the incident energy changes, and find that it changes in character above a critical energy E_c, at energies less than E_c the ambiguities occur, but for higher energies they are extinguished

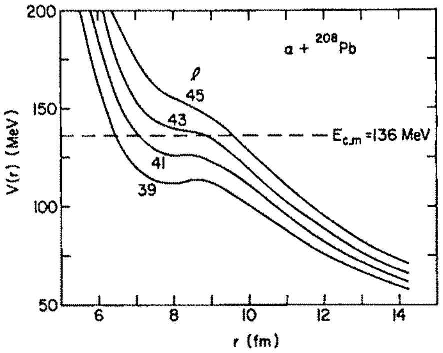


Fig. 1 Effective potentials for the elastic scattering of alpha particles by ^{208}Pb for values of l around 43

To see how this comes about, recall that the differential cross-section may be expressed as a function of the phase shifts so that ambiguous potentials must give very nearly the same phase shifts for all the partial waves that contribute to the scattering But a phase shift is an angle, so increasing or decreasing it by any integral multiple of π does not affect the cross-section Thus if all the phase shifts below a critical value l_c of the orbital angular momentum increase by $n\pi$ the ambiguity can occur

This can happen for helion and alpha-particle scattering, as shown in Fig 1 The total effective potential $V(r)$ acting on the incident particle of orbital angular momentum l is the sum of the nuclear potential, the electrostatic or Coulomb potential and the centrifugal potential $l(l+1)/r^2$ and this is shown as a function of r for several values of l for alpha particles on ^{208}Pb These particles are strongly absorbed, so the scattering is essentially determined by the potential beyond the classical turning point defined by the condition that the incident energy equals $V(r)$ Now if the position of the turning point is regarded as a function of incident energy for different values of l, it can be seen from Fig 1 that it moves inward suddenly at an energy corresponding to the triple point at which the minimum in $V_l(r)$ disappears This sudden movement of the classical turning point at a critical value of l allows the phase shift to increase by $n\pi$ and hence gives rise to potential ambiguities

The connexion between this sudden movement and the ambiguities is shown in Fig 2 Here several different potentials all giving essentially the same differential cross-section are plotted as a function of radial distance for the critical partial wave with l=43 For each potential, the turning point moves in suddenly by amounts corresponding to phase shift increases of π, 2 π and 3 π The ambiguities persist for all values of $l<l_c$, but at energies higher than E_c they do not arise, because there is no sudden dip in the effective potential and hence no sudden inward movement of the turning point For energies less than E_c the ambiguities therefore occur in all partial waves, and thus in the potential as a whole, whereas for energies greater than E_c they do not occur in the higher partial waves It is not possible in the latter case to find a potential that reproduces both the smooth variation for the higher partial waves and the $n\pi$ increase in the phase shifts for the lower partial waves, and so the potential is unique It is thus possible to understand why the potentials show ambiguities at low energies but not at high energies, and to relate the critical energy to the form of the effective potential

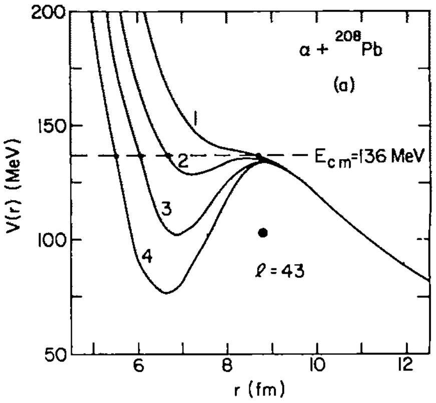
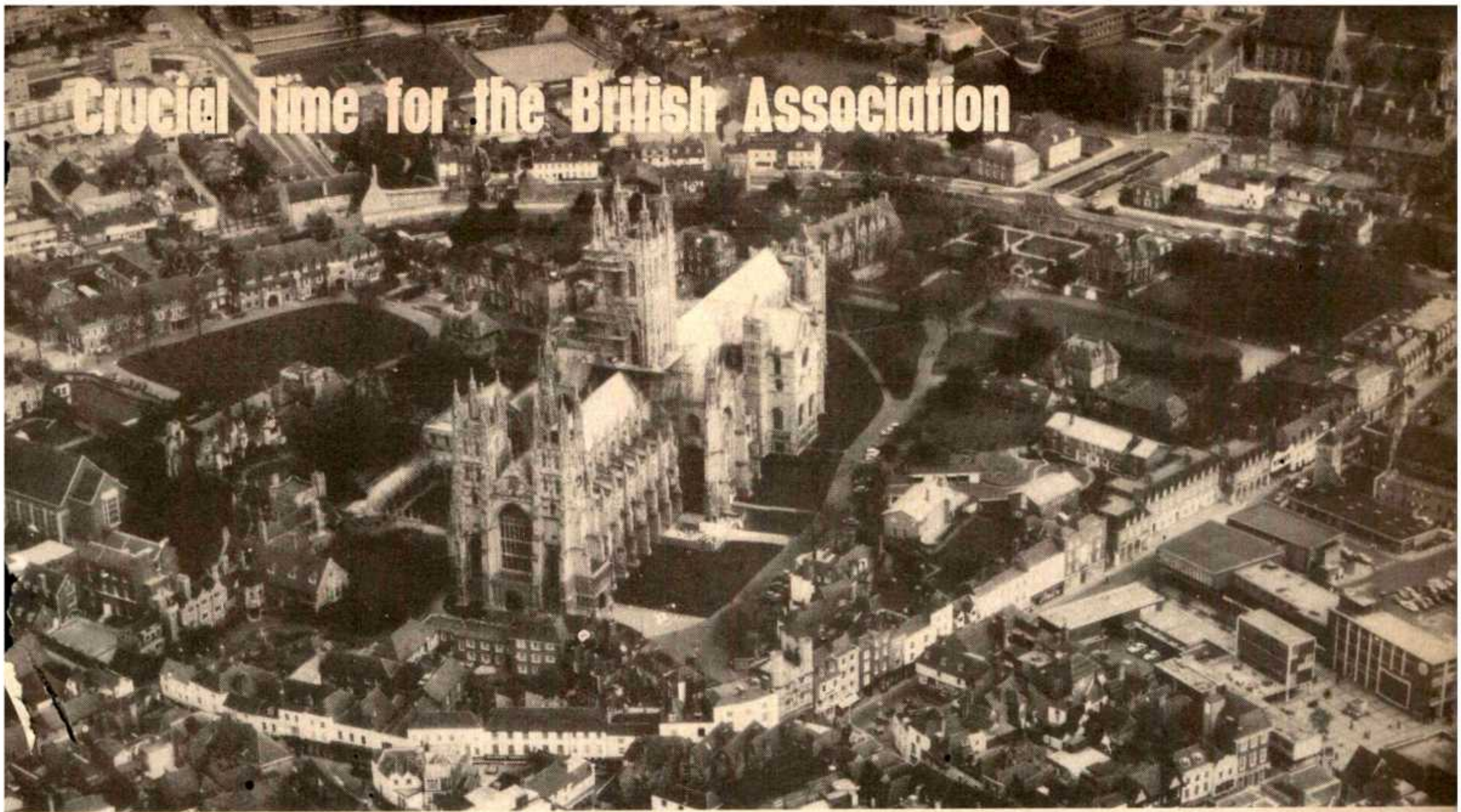


Fig 2 Effective potentials for the elastic scattering of alpha particles by ^{208}Pb for l=43 only Each of these potentials gives the same scattering, showing that the phase shifts differ by $n\pi$

Correction

IN the News and Views article "Receptor Function" (*Nature*, **244**, 253 , 1973), the penultimate sentence in the third paragraph should read "Moreover, during successive ACh applications, the toxin becomes completely effective only after the first contact with ACh, suggesting that its action is dependent on an initial binding of ACh at the receptor " In the published version the word "effective" unfortunately appeared as "ineffective"

Crucial Time for the British Association



Canterbury [*Aerofilms Ltd*]

THE British Association for the Advancement of Science is breaking new ground once again at its 135th Annual Meeting which is to be held at the University of Kent at Canterbury next week. Through no fault of its own the association is holding its annual meeting in mid-August instead of the traditional time of early September, which might well put back its plans to increase the popularity of the meeting. And it is only a year since the association, in an attempt to shake off its rather lacklustre image, made another break with the past when it decided to compress the annual meeting into a week beginning on Monday instead of spreading the delights over the best part of two weeks with a relaxing weekend in between.

These outward signs that the association is serious about coming to terms with the 1970s do not constitute the entire story, for the most significant changes have been taking place behind the scenes. Since the annual meeting at Leicester last year the Privy Council has approved drastic changes in the association's constitution which, for one thing, will turn the gargantuan general committee into a more manageable body of close on sixty members, more than half of them being elected. This committee will have the powers to elect a council of twenty-two members which will have as its chairman, for the first time, a paid officer of the association. These changes will be instituted, not before their time, after the annual meeting next week and there is little doubt that the association from now on will be a much more wieldy body that should be a better barometer of thoughts and concern in Britain about science and its implications.

As luck has it, the streamlined BA is now in a good position to fight off the challenge, and that is what it is, from the newly formed Council for Science and Society which was set up with generous support from the Leverhulme Trust (see *Nature*, **244**, 191; 1973). The stated aim of this council is to identify areas of research with important social consequences and to study these objectively. The comparison of this new council with the much criticized British Society for Social Responsibility in Science is clear, but there are also obvious clashes between its aims and those of the BA. The Royal Society grant to the BA—which amounts to £20,000 a year—is ostensibly for the purpose of "the popularization of science and the conducting of a responsible public debate on the social consequences of science". And it must be asked whether, in the long run, this competition—if it will develop—will do the BA more good than harm. This is the question which will be at the front of the minds of delegates to the conference this week. The BA has a head start on the Council for Science and Society and the first reports of the association's investigations, instigated in 1972, to look into matters of scientific concern should be available early in the new year. It is, however, essential that the momentum which has been generated by these investigations into the social consequences of research in biology and genetics and into the place of research in higher education in Britain should be maintained by other studies, and it is significant that the association has now put the responsibility of choosing topics for investigation on to its executive committee.

But the BA is best known for its annual meeting which has been held during all but six of its 141 years of existence. Last year the meeting, to be blunt, attracted rather less support than anyone would wish and it remains to be seen whether the enforced change of date to the middle of the holiday season will boost attendance. The association, after a great deal of soul searching, has decided to persevere with the annual meeting, a decision to be admired, but it is to be hoped that as time goes on that the meeting becomes less of the centre of the universe as far as the association and its members are concerned and that other activities will come into their own and receive due attention.

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Good Times Just Around the Corner for Nuclear Power?

by our Special Correspondent

Nuclear power may finally be about to come into its own. This article examines the past and glances at the future of the industry and the United Kingdom Atomic Energy Authority.

"WITHIN ten to fifteen years we may have reached the point at which every new power station will be a nuclear power station". Those words were not uttered this year. Or last. Indeed, they are a prophecy that was so far from being true that fifteen years after they were said, the nuclear industry in Britain was entering one of the leanest periods in its chequered history.

These words in fact are Sir Edwin Plowden's, the first chairman of the UKAEA. And they were spoken in 1956, the year Calder Hall, the world's first nuclear power station, opened. But in spite of the fact that the targets set in the 1950s and 1960s in Britain's first and second nuclear power programme have not been met, future prospects are now much brighter. It is now likely that in fifteen years time almost every power station ordered will be nuclear.

In the years in between Sir Edwin's statement and now, the history of atomic energy in Britain has not been an entirely happy one. There have indeed been times when the critics of the nuclear industry and the Atomic Energy Authority in Parliament, the press and industry, have seemed with ill-disguised glee to be siding with Nöel Coward's three equable businessmen in cheerfully declaring that there are bad times just around the corner.

Why has it taken so long for nuclear power to be on the verge of dominating future orders? And indeed, what part has the UKAEA—the source of those optimistic forecasts of the fifties—played and still got to play in nuclear power? Controlled nuclear energy had its origins on December 2, 1942, in Chicago. On that day the first uranium-graphite pile was operated and man had initiated a self-maintaining nuclear reaction for the first time. Less than fourteen years after that Calder Hall was feeding electricity into the national grid in Britain. In between the Atomic Energy Project and then the UKAEA were set up.

The prime mover was defence. Britain wanted nuclear weapons and in 1946 Harwell was established and the British scientists who had been in North America during the war, helping in the work that led to Hiroshima and Nagasaki, came home. Air-cooled graphite-moderate piles were built at Windscale to produce plutonium, Aldermaston did its calculations, and in October 1952 the Monte Bello test was fired.

But while controlled atomic energy was born in war the possibilities of power generation were realized before then. By 1949, however, it was thought that the only worthwhile early application of atomic energy would be submarine propulsion. Electricity generation using enriched fuel, it was agreed at the time, would not be economic. But in 1950 the possibility of using natural uranium fuel to produce both power and plutonium was realized, and in January 1951 a design study started. The first results were presented at the Harwell Power Conference of 1951 and were heavily criticized. The size and cost of the proposed reactor were both attacked, the advantages of sodium cooling over gas cooling were emphasized, and the Risley team pressed for all the effort to be put into fast reactors. Incredibly, looking back, the natural-uranium reactor was dropped from the first draft of the 1952 Harwell programme. If that decision had been upheld the face of nuclear power in Britain today would have been radically different. As it was, the design that was to become Calder Hall was rescued by Mr B. L. Goodlett, deputy chief engineer at Harwell, and Mr R. V. Moore, now managing director of the Reactor Group.

In Richard Moore's words, "By the end of 1952 it was certain that a design had been produced which could and should be built". In February 1953 approval was given for the construction of Calder Hall, a Magnox type reactor. British industry—under the authority's management—demonstrating what can be done when the pressure is really on, built the first half of the station in 33.5 months, completing the second half 6 months later. The end result was primarily a factory to produce plutonium, with power also available as a byproduct.

But while Calder Hall was being completed the first nuclear power programme was announced in 1955. Twelve power stations with a total output of between 1,500 MW and 2,000 MW were to be built in the ten years to 1965. In 1956 the Suez crisis occurred, and the next year the Government reacted to the possibility of Britain being cut off from its oil supply by trebling the nuclear programme. In all, between 5,000 and 6,000 MW were to be installed by 1965. But in October of 1957 the expansion had to be ignominiously rephased as part of restrictions of capital spending and the target date was extended to 1966. In 1960 it was further extended to provide for 5,000 MW by 1968. In fact, excluding Calder Hall and Chapelcross, reactors originally built for plutonium production, Britain managed to achieve only 4,856 MW of installed capacity by August 1971 when Wylfa, the ninth nuclear power station to be built, came on full load. To add to the confusion of planned, rephased and postponed programmes, the second nuclear power programme which was announced in 1964 was intended to provide an additional 5,000 MW of nuclear capacity using advanced gas cooled reactors between 1970 and 1975. This target was raised to 8,000 MW in October 1965, and "for planning purposes" it was assumed that on average over the six years 1970 to 1975 one nuclear power station would be commissioned every year. So far, none of these stations is operative. It is a fairly depressing story. And looking back the mistakes loom large. The panic expansion of the programme in 1957, followed by the stop, go and rephase policies of government, produced a degree of disruption that few industries could cope with, and certainly no industry as poorly put together as the nuclear one. Its shape was wrong from the start. In 1954 no less than four industrial consortia were formed to design and build nuclear power stations, and in 1956 a fifth consortia was added. Despite the steady pruning of the consortia—forced largely by commercial necessity rather than by the desire of the CEGB to deal with only one consortium—the result has been that almost every nuclear power station has been, in effect, a prototype. Hunterston B, the AGR station being constructed in Scotland, is the first repeat order for a nuclear power station. All the earlier stations were significant modifications of their forerunners. Many of the problems that new stations have run into should hardly come as a surprise. Added to this are the technical problems—particularly the steel corrosion problem which has cut the output from some of the Magnox stations by almost 20%.

The other fundamental error lay in ordering the AGRs more or less from the drawing board. The Windscale Advanced Gas Cooled Reactor—which celebrated its tenth anniversary of successful operation earlier this year—is not a full prototype, being designed largely to develop materials and fuel for the commercial stations. The result was three prototype AGRs being built at Dungeness, Hartlepool and Hinckley by three different consortia with all the attendant problems. The current contraction of the industry into just one consortium—which even the Select Committee on Science and Technology saw the need for in 1967—is a much needed remedy. But while the nuclear industry has been forming and reforming itself and while its power stations fell behind schedule and went over budget, what has the UKAEA been up to?

The authority has changed greatly in its eighteen year life. Defence brought it into being, and defence preoccupied it to a greater or lesser extent for its first ten years. Production of plutonium for nuclear weapons led to the building of the "atomic factories" at Windscale, Springfields and Capenhurst and to the large staff of the authority. Once Calder Hall became a reality the UKAEA had the job of underpinning the design and construction of Magnox reactors, followed shortly by the development of other reactor systems. The Dounreay Fast Reactor, the Advanced Gas Cooled Reactor, the Steam Generating Heavy Water Reactor and the High Temperature Reactor were all studied and developed, and the UKAEA's expenditure and manpower rose rapidly to a peak in 1961–62 (see Fig. 1). But by the mid-1960s, questions were being asked. Between £750 and £800 million of taxpayers' money had been spent by the authority (some of it on defence work) and all Britain had to show for it, the argument ran, was three working power stations and six more under construction.

Further, it was becoming increasingly clear that much of Harwell's work on neutron physics and other applied research on the basic aspects of reactors was, if not nearing completion, at least falling in scale. Yet the authority contained a great deal of expertise in many fields that simply could not be disbanded. An added complication was that the production side of the authority, having produced as much plutonium as Britain's navy and air force could hope to deliver in the event of war, had turned itself into a highly effective fuel organization which was making money—an aspect of the authority's work that a select committee of Parliament felt was rather at odds with its research and development role.

The result was the Science and Technology Act of 1965 which freed the authority to undertake non-nuclear work and which set up the Trading Fund, a commercial profit and loss account that charted the progress of the fuel and radiochemical sales of the UKAEA.

The changes were important. In 1971 the trading fund was taken to its logical conclusion and British Nuclear Fuels and The Radiochemical Centre were formed as separate companies.

To prove its value to the country and to help offset the cost of running the authority, the AEA has put considerable effort into its contract research, and in 1971–72 its income from non-nuclear and nuclear contracts totalled about £8.5 million. Harwell, for example, now has its work divided up into four roughly equal parts—studies of specific problems on reactor development, examination of long term scientific problems, contract work for industry and contract work for government departments, while Risley earned £3.75 million in foreign currency for contract work last year.

While this side of the authority's activities has grown, the overall size of the organization has fallen steadily, and the reorganization of the fuel and radiochemical side, allied with transfer of Aldermaston to the Ministry of Defence in April this year, has left the authority—on paper at least—a more rational organization than it appeared to be a few years ago.

But what of the future? In spite of the black facts of Britain's nuclear past, the signs are now that nuclear power may be about to meet the promises of the fifties. And for reasons similar to those that set the first nuclear power programme under way. The price of oil—already at close to $3 a barrel and likely to rise further now that the United States can no longer meet its own needs—augurs well for a future that will have to be largely nuclear. Coal, while plentiful, is unlikely in the immediate future to be minable at a low enough price and in sufficient quantities to meet the growth in energy demands. It is not insignificant that the cheapest electricity generated last year by the CEGB came from some of the nuclear stations. It is equally possible that nuclear stations may prove to be longer lived than the twenty year design life given to Magnox stations.

And once the government has announced which type of thermal reactor is to be built next—and the indications are that it may be another AGR—industry should be able to drag itself out of a three year doldrum in which it has not had a new nuclear order. The long period of stagnation has done no good, but now that the industry is organized into one company—the National Nuclear Corporation—the future has to be brighter.

A new station will be ordered next year, followed by perhaps a further half dozen stations during the 1970s, with orders coming at the rate of three to four a year in the 1980s if the economy behaves itself and follows its predicted path. The first fast breeder order is theoretically due next year. In fact it is unlikely that an order will be placed until the prototype fast reactor at Dounreay, which is currently being commissioned, has proved itself.

There are also indications that we may have learnt from past mistakes. One of the chief problems with the Magnox stations was transferring the technology to industry. With the fast breeder The Nuclear Power Group has been involved in the design and development work since 1969, and, until the reorganization of the industry was announced last year, it was the group that was to build the first commercial fast reactor. The new National Nuclear Corporation will now do that, but doubtless with TNPG's staff. It is also intended to build just one commercial fast reactor design to start with, avoiding the old problems of too many prototypes. Equally, some of the lessons from the AGR programmes have been learnt and the Dounreay PFR has a number of features—for example, the size of the fuel rods—which could be used in a 1,000 MW commercial station as well as in the 250 MW prototype.

The other key lesson that must be learnt is that industry must be able to build the stations to time and budget if nuclear power is really to pay. The first nuclear programme was planned to cost £300 million and in fact cost £750 million. The CEGB has come tacitly to accept that it takes up to seven years to build a station, and the overruns on the AGRs are horrifying—the cost to the CEGB being enormous. The Japanese company Mitsubishi is said to offer to construct nuclear stations in forty-eight months. While that figure may not be ideal—it is more important that stations are built late and safe than early and sorry—it is still a level of competition worth bearing in mind if Britain's nuclear company is to be a commercial success in foreign markets as well as at home.

But once the new thermal reactor has been chosen, and once the fast breeder is being built by industry—and the design for a commercial station got under way while the prototype was still being built—what will there be for the UKAEA to do? A favourite argument has been that industry will simply have taken over. The authority will have to be disbanded. But many arguments militate against this.

In the short term there is a lot of work to do. Whichever

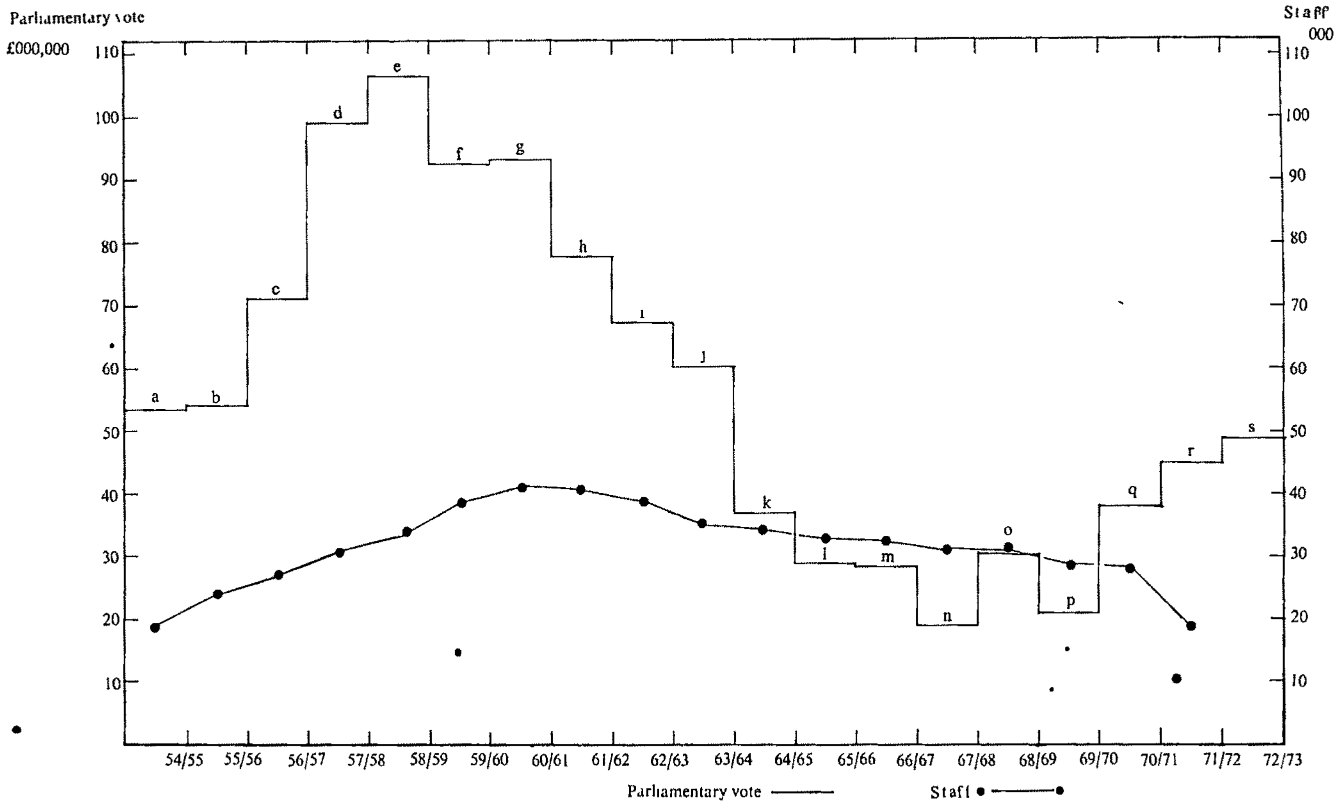

Fig. 1 The UKAEA the cost to the country*

(a) Work on Calder Hall and Dounreay Fast Reactor already under way Dounreay started March 1955, Calder Hall March 1953 First Nuclear Power Programme announced February 1955 twelve stations in ten years for £300 million Four consortia formed Design of Zeta begins (b) June 1955 six more reactors for military plutonium production approved Two more reactors for military plutonium production approved Two more for Calder Hall, four at Chapelcross (c) October 1956 Calder Hall opened Work on Berkley and Bradwell power stations starts in January 1947 A fifth nuclear consortia formed and the revised nuclear programme (5–6,000 MW by 1965), announced Development of reactors for submarine propulsion begins February 1957, National Institute for Research in Nuclear Science established (d) Britain's first megaton range nuclear weapon exploded at Christmas Island, May 1957 August 1957, Zeta on full power Winfrith establishment set up Construction of 7 GeV proton synchroton begins at Rutherford High Energy Laboratory International Atomic Energy Agency established Construction of Hinckley Point A and Hunterston A begins Windscale accident releases radioactivity to atmosphere, October 1957 (e) Construction of Windscale prototype AGR begins First Chapelcross reactor begins feeding electricity to grid, February 1959, last Calder Hall reactor critical, December 1958 Springfields manufactures its millionth fuel rod Twelve European countries sign agreement to develop Dragon High Temperature Reactor Dounreay fast reactor completed United States pressurized water reactor bought to power Dreadnought submarine (f) Construction of Trawsfynnydd power station begins Major defence projects completed and all main defence plant commissioned Capenhurst diffusion plant extensions completed and DFR on power (g) Culham laboratories established June 1960, nuclear power programme timetable extended August 1960, Dungeness A under construction, April 1961, Sizewell B started Second nuclear submarine ordered Five consortia reduced to three by mergers (h) Windscale AGR completed First Nevada underground test, March 1962 Oldbury A power station construction started (i) Berkley and Bradwell Magnox stations on load Latina nuclear power station in Italy—designed by The Nuclear Power Group—on load Windscale AGR begins generating electricity Construction of SGHWR begins Second Nevada test Fall in enriched uranium requirements for defence leads to 50% cut in Capenhurst staff Nuclear marine propulsion being studied with view to building prototype ship (j) Production of U-235 for military purposes stopped Greater part of capital works programme complete Wylfa power station construction begins October 1963 Dragon goes critical (k) Hunterston A, Hinckley Point A and Trawsfynnydd on load Second Nuclear Power Programme announced (AGRs) Millionth magnox fuel element produced at Springfields Science and Technology Act provides UKAEA freedom to undertake non-nuclear work Trading Fund set up to run commercial fuel and radiochemical work as self-financing account National Institute for Research in Nuclear Science transferred to the Science Research Council Marked drop in grant due to NIRNS transfer, trading fund, and to Ministry of Defence providing eight annual payments to cover capital liabilities outstanding on military plants and the terminal expenses of closing down production (see i and j) First payment £37 7 million (l) Dungeness B ordered Fuel policy white paper foresees one nuclear station a year to be commissioned between 1970 and 1975 Capenhurst modernized to provide AGR fuel Construction of Prototype Fast Reactor approved Marine propulsion reactors rejected for immediate development, but studies to continue. Underground test at Nevada Authority unsuccessfully bid to build SGHWRs for two Finnish utilities (m) British Nuclear Export Executive formed to sell reactors overseas Sales promotion in Belgium, West Germany, Rumania, Austria, Switzerland, Greece, Finland, Japan (n) SGHWR completed PFT construction under way Hinckley Point B and Hunterston B ordered Work on fusion to be cut 10% per annum for five years Tokai Mura Magnox Station in Japan, built by GEC–Simon Carves, on load (o) Consortia cut to two—British Nuclear Design and Construction and The Nuclear Power Group TNPG brought in to work on PFR Forty authority staff transferred to the consortium and 100 others seconded PFR programme put back a year due to difficulties in manufacturing radiation shield roof (p) Legislation to form British Nuclear Fuel and the Radiochemical Centre Ltd prepared, but not passed as Parliament dissolved in 1970 Green Paper proposes a British Research and Development Corporation intended to take over staff of research and reactor groups together with five MinTech establishments and the National Research and Development Corporation Urenco and Centec set up to build gas centrifuge enrichment plant at Capenhurst and Almelo British Nuclear Export Executive, no reactor sales to its name, disbanded Culham staff in USSR for fusion experiments on Tokomak (q) BNFL and Radiochemical Centre Ltd established Desalination plant at Ipswich approved National Radiological Protection Board set up and authority Safety and Reliability Directorate formed Thermal Reactor Review under Peter Vinter examines choice of next reactor type Heysham AGR ordered (r) Period of animated suspension while government ponders the future, the authority develops all its reactor types and the industry looks at its emptying order books Ipswich desalination plant abandoned (s) Formation of one nuclear company announced Further eighteen months of studies before decision on next reactor type to be taken Fusion research stepped up

* Source UKAEA annual reports, reporting years run April 1 to March 31

thermal reactor type is chosen, the UKAEA will have to underpin the development of it by industry Should light water reactors be chosen there will be at least two or three years work to be done on design before a station can be built—and the authority will certainly have plenty to do on the thorny question of safety Work on the High Temperature Reactor will undoubtedly continue and the authority should be able to redeploy its resources, which, it maintains, are being stretched by the need to keep so many reactor types under detailed study, into whichever reactor type is chosen And there is still a lot of underlying work to be done on the fast breeder—perhaps very different from the neutron physics work of the early days, but work on high temperature steels and other work fundamental to component development

In the longer term lies fusion Expenditure and effort on fusion work has just been stepped up again and the UKAEA is preparing a cooperative programme with Europe Fusion has had a tough time in Britain—suffering most from the extreme and, it proved, unfounded optimism that accompanied Zeta's early results in the late 1950s In 1967 it was decided to cut expenditure by a half over a five year period and disillusion with the hopes of fusion had really set in Culham entered into the contract research business, but this year's decision to increase expenditure and to design a large experiment has put the impetus back into fusion A rough timescale for the development of fusion could be that a large experiment to investigate plasma physics will be built for 1978, followed by a larger machine to study a plasma sustained by thermonuclear reactions and refuelled with cold fuel, a system that could perhaps be followed by a prototype generating plant Such a timescale —if all goes well and controlled fusion in fact proves possible—could produce fusion reactors by about 2000

The longer term may also include the development of other reactor types A glance at history suggests that it would be foolish to assume that the sodium cooled fast breeder, promising though it now looks, is the ultimate in fission reactors The gas cooled fast breeder is just one other possibility on the horizon

Most importantly though, the authority will still need to do the fundamental safety work on all reactor systems When the decision is taken to build a reactor all the questions about its safety have not been answered for all time The possibility of a nuclear power station accident is not to be treated lightly, and it is fundamentally important that the assumptions on which the proclaimed safety of nuclear power stations is based are continually re-examined

But safety research does not show a profit, and it cannot easily be left to the nuclear company—particularly if the decision is taken to develop High Temperature Reactors internationally and in industry rather than in the relevant government undertakings—to fully question the safety of its nuclear plant The need for a body to undertake such research—and studies on the long term reliability of nuclear stations which involve huge capital sums—combined with the need for fuel and waste disposal research guarantees the authority a role It will be a much changed role from the days when the authority handed down the nuclear lore to British industry Indeed it may largely consist of acting as a contract research organization for the industry and the generating boards, but it could be a role that will do much to ensure that Britain really does profit from nuclear power

Whither Climate Now?

H. H. LAMB

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Since Professsor Lamb wrote on "The New Look of Climatology" (*Nature*, 223, 1209; 1969) he has set up a research unit in the University of East Anglia for study of the long-term behaviour and current trends of climate.

SURFACE air temperature averaged over the globe seems (Fig 1) to have been falling since the 1940s, at least up to 1969 Temperatures at lowland sites typical of central England, averaged over the year, also fell successively from the peak value of 9 7° C in the 1940s to 9 5° C in the 1950s and 9 3° C in the 1960s, thereby returning to the average level of 1910–30 or, for that matter, to the average for the hundred years 1851–1950 In the Arctic the recent downturn has been far greater (as was the warming in the 1920s and 1930s) and remarkably abrupt At the observation post in Franz Josefs Land (80° 20′ N, 52° 48′ E), which was for long the station nearest the North Pole, ten-year average temperatures from the beginning of the permanent record in the late 1920s up to 1960 varied between −10 8 and −10 0° C, for 1960–69 the figure was −14 5° C

Figure 2, using a crude but readily available measure of the temperatures prevailing over the main ice-producing areas of the Arctic Ocean, indicates that the lower temperatures which set in abruptly about 1961 in that region have been continuing right up to now despite the fluctuation which has given three mild winters in England since 1970

A survey covering as much of the northern hemisphere as could be analysed from 1881 to 1960 for the incidence of extreme warm and cold months[2], with mean temperature departing by ≥10° C from the overall average for the same months (all in the cooler seasons of the year), showed the extreme positive departures concentrated in the higher latitudes, particularly over Siberia north of the Arctic circle and over west Greenland (in each of which areas there were ten extreme warm cases in the eighty years and no extreme cold cases, except east of 140° E)

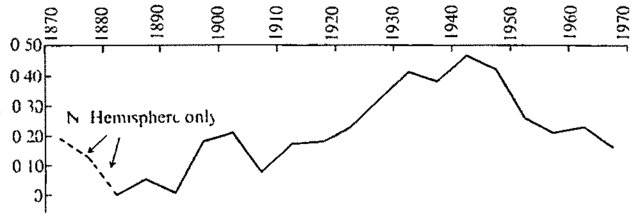

Fig 1 Changes in global mean surface temperature (five-year averages from 1880–84 to 1965–69, after J M Mitchell and NCAR) - - -, Northern hemisphere only

This distribution was evidently associated with the warming of the Arctic and recession of the sea ice which was proceeding most rapidly in the 1920s and 1930s The extreme cold months in those early years were concentrated in the central regions of the continents of Asia and North America between latitudes 40° N and 65° N But since 1960 there have been many of

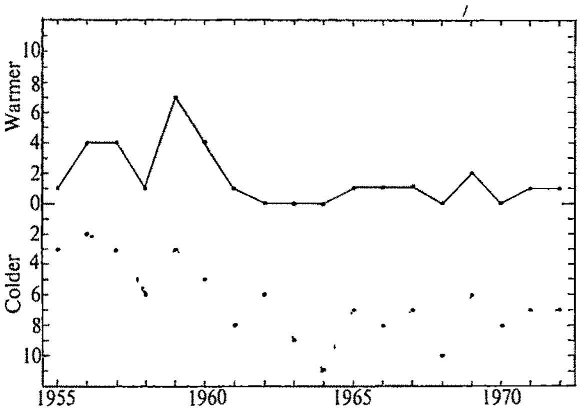

Fig. 2 Numbers of months each year from 1955 to 1972 in which most of the region north of 70° N appeared warmer (——) or colder ( ) than the 1931–60 average Data compiled from the monthly maps of surface temperature anomaly published in ref 1

these anomalously cold months in the Franz Josefs Land sector of the Arctic, the extreme case (January 1964) at that point having a mean temperature 18° C below the 1931–60 average

An important feature of this climatic change seems to have been a change in the general atmospheric circulation Before 1960 a circumpolar vortex with at most two persistent cold troughs in high latitudes, generally over northeast Canada and northeast Siberia, was characteristic Since then the monthly patterns have rather frequently shown three troughs, the extra trough being mostly in the Franz Josefs Land–Novaya Zemlya sector Its introduction has meant greater amplitude and shorter wavelength in the meandering flow of the upper westerlies and, presumably, some net expansion of the cold area of the polar cap bounded by the strong flow of the upper winds The greater northward and southward excursions of the surface and upper winds over middle latitudes and the sub-Arctic fringe that go with such patterns have produced some extreme warm as well as extreme cold months in latitudes between 40° N and 70° N and an abnormal incidence of blocking anticyclones

The decline of the westerlies in Britain (Fig 3), the extreme warmth and dryness of summer 1972 in European Russia with a three-month mean temperature nearly 5° C above the 1931–60 average near the Finnish border, and the mild dry December and January 1972–73 in Scandinavia and central Europe (with little snow at many winter sports resorts and roses flowering in late January in Copenhagen) all fit into this pattern The same month of January 1973 saw the Labrador ice belt extend beyond its previous record east of Newfoundland and equalled the lowest temperatures observed in the past 140 years at Sverdlovsk in the Urals at 60° E No doubt this type of behaviour of the large scale circulation of the atmosphere underlies the fact that twelve of the fourteen warmest Januarys in England since 1680 fell within four years of a January with mean temperature below 2° C, six of them within either one or two years of such an opposite extreme This is also bound up with a serious difficulty that attends many of the rules derived by statistical significance tests for long-range weather forecasting the same conditions which precede severe winter in Europe also show a certain enhancement of the frequency of abnormal winter warmth, usually attributable to the sector affected by southerly winds on the western side of a persistent blocking anticyclone

The increased extent of the Arctic sea ice since 1961 caused understandable alarm in Iceland, which was half surrounded for a time in 1968 But in the past two years the excess ice has been concentrated west of Greenland and in the Canadian sector, the east Greenland ice belt has narrowed again but has consisted of heavy "polar" ice

These variations have excited interest in the popular press as well as in scientific circles, but particularly in those regions which at any given time have happened to be most adversely affected With three mild winters in a row since 1970, the longest run of mild winters since 1948–50 in Britain and much of northern Europe (though, at least in England, not overall as mild as those of twenty-three years ago), concern over the trend of our climate seems to have died down And it may be partly for that reason that the newly established Climatic Research Unit in the School of Environmental Sciences at the University of East Anglia is seriously short of the financial support needed for its continuance

Nevertheless, the instability of the climatic regime and the possible threats to it from side-effects of man's activities[3,4] are more widely appreciated than before And it is safe to predict that the next season of adverse weather will bring a clamour of inquiries and requests for climatic forecasts that we should prepare to meet

The working group on climatic fluctuations set up by the World Meteorological Organization in 1969, with myself as chairman, had as the main items on its agenda to consider the causes, both natural and man-made, of climatic changes, the demand for advice on future climate and the ability of science to deal with this demand

The demand confronts meteorological services in all the advanced countries, and many others besides, with a problem that the science is admittedly ill-equipped to meet It has arisen from the needs of practical decision-making in connexions as various as the provision of adequate supplies of electricity and fuel oil, the incidence of drought in arid lands with rising populations and increasing industrial use of water, shipping insurance against hurricane damage, the future of the Atlantic and Arctic fisheries, forest planning at the northern limit in Finland and in the Solomon Islands where the threat is from tropical cyclones All these have been affected by the climatic trend since 1950, and in several connexions vulnerability is increased by man's systematic exploitation of the natural resources (particularly water) of the area concerned to the limit

To develop a scientific approach to the problem of prediction—or, more modestly and realistically stated, of advising on future climatic probabilities—the first essentials clearly are (i) to establish the facts of the past climatic record in as much detail, over as much of the Earth and as far back in

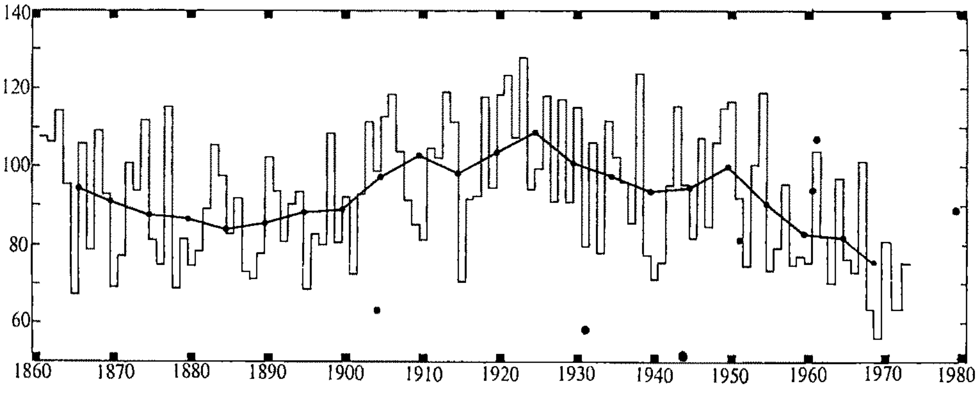

Fig. 3 Number of days per year of general westerly type over the British Isles (1861 to 1972) ——, Ten-year means, plotted at five-year intervals (and the latest ten-year mean 1963–72)

time, as the data permit, and (ii) to use this observational record to diagnose the processes at work in bringing about climatic changes If we are to identify any recurring processes which take many years, and in some cases centuries, for their completion, it is axiomatic that we need the longest possible observational record

Identification of the circulation processes in the atmosphere and oceans, and of any cyclic changes in the water stored as ice and snow on land and in the soil, as well as of any other relevant physical changes (volcanic dust, ozone, carbon dioxide, and so on) in the atmosphere, or in the Sun or the cosmic environment, will require techniques ranging from time-series analysis of the very long climatic records to mathematical modelling of the atmosphere and hydrosphere and many new types of observation (such as of oxygen and carbon isotopes) Some leading meteorologists in various countries today maintain that the problems of long-range weather forecasting on any time-scale will only be solved by mathematical modelling techniques, that there is no convincing evidence of any variability of the solar output (though the series of direct observations are somewhat short for such confidence) and that there is little point in attempting to reconstruct the past record of climate in any detail At the other extreme, a conference held at Brown University, Providence, Rhode Island, in 1972 attended by geologists, palaeobotanists, marine biologists and others, including representatives of the oxygen isotope laboratories, two leading meteorologists and a physical oceanographer, took as its theme "The present interglacial, how and when will it end ?" The verdict favoured by the majority[5] was that "the natural end of our present warm epoch is undoubtedly near Global cooling and related rapid changes of environment substantially exceeding the fluctuations in historic times, must be expected within the next few millennia or even centuries "

There is a manifest psychological difficulty in bringing together the type of mind represented by the different attitudes among scientists mentioned in the previous paragraph But it must be done And perhaps the most helpful of all avenues of research towards reaching a balanced understanding is to seek out the facts of the past climatic record As T H Huxley wrote, one must "sit down before fact as a little child" The actual record of the past is, after all, vital to test the realism of the mathematical models

The Climatic Research Unit at Norwich aims to map and publish the ascertainable facts of climate and circulation patterns prevailing year by year over the period of historical documentation, both before and after the introduction of meteorological instruments, and to work on meteorological analysis of the average conditions of more remote periods for which the data are derived from many kinds of fossil evidence In this work, liaisons with the most diverse branches of science and learning must be cultivated The CRU also reviews at regular intervals the current development of climate and experiments with methods and formulation of forecasts covering periods from some months to many years ahead

It is known that several bodies in various countries engaged in activities involving planning for up to fifty years ahead have devised their own methods of arriving at the projections of future climate which they need and that some scientists have also produced forecasts for a similar length ahead These forecasts have so far been based on one or other single line of evidence and have doubtless been regarded as less than satisfactory for this reason by their originators Surprisingly, however, there is (as is probably quite widely known) a concensus among them of a trend towards a cold climate in the last decades of the present century

There is an obvious need, and it is among the aims of the Climatic Research Unit at Norwich, to bring the various forecasting methods together, to review their physical assumptions and test their statistical basis with new data and so develop a wider understanding It is hoped, in particular, to make progress by identifying quasi-periodicities in meteorological and climatic data and relate them to the evolution of the global atmospheric circulation at the different phases of each It should then be possible to recognize interrelationships which are not at present understood and to monitor each current cycle with an eye to anomalies and interference phenomena affecting it To do this, it is necessary to set the long-term observational base of climatology on a firm footing And it will be in pursuit of this that the Climatic Research Unit will make its first, and perhaps most distinctive, contribution

A start has been made with building up an archive of historical observation data Handsome gifts have been received from the remarkable wealth of early data from northern countries in the possession of the Danish Meteorological Institute The help and advice of the Netherlands Meteorological Institute and of individual scientists in Germany, England, the United States and Japan, as well as of historians in France, Denmark and Norway, are also gratefully acknowledged For the analysis of the climates in prehistoric times promising liaisons have been established with seven American universities, and with the sub-department of Quaternary research in the University of Cambridge as well as with the oxygen isotope laboratories in Cambridge and Copenhagen An international meeting of research workers concerned with mapping the climatic patterns of the last ice age was held in the University of East Anglia in May 1973

Compilation and meteorological analysis of the January and July maps of individual years from AD 1680, and compilation of seasonal data on maps back to AD 1200, begun when I was on the staff of the Meteorological Office, have proceeded far beyond the pilot stage, and the feasibility of the projects with these maps is established The combination of linguistic, historical data sifting and meteorological talents required, and access to the great data banks in the Meteorological Office, Bracknell, and in the libraries in Copenhagen, London and elsewhere, is probably uniquely present in the staff of the CRU at Norwich, but the carrying through of the project is unhappily threatened by the present lack of financial means to continue employing the staff beyond 1975 or to provide the necessary ancillary posts

Work at Norwich on the monitoring of the current development of the climate is at present limited to assembling data covering the northern and southern hemispheres that have already been collected and published by various meteorological services, to considering and analysing the data in various ways and to publishing a global digest based on this (CRUMB—Climatic Research Unit Monthly Data Bulletin) The unit is greatly indebted to the National Oceanic and Atmospheric Administration, the United States Air Force, and the Smithsonian Institution in Washington for gifts of daily weather maps of the northern hemisphere covering the present century and tabulated monthly climatic data for reference covering the past 100 years or more, and enjoys exchange arrangements with the Meteorological Office and the Deutscher Wetterdienst for analyses of the most recent observational material Experimental forecasts are formulated several times a year and the results are to be assessed yearly When the staffing position permits, it is hoped to stage a series of meetings to elaborate "forecasts" using exactly similar information and methods for years and seasons that are already past (and forgotten)

Once we have a secure base it will be possible to broaden our activities in monitoring current climate in many ways There are plans for studies of the direct effects of certain types of pollution on climate, the effects of afforestation and of urban development, and the longer-term exchanges between sea and atmosphere over the northern seas

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[1] *Die Grosswetterlagen Europas* (Deutscher Wetterdienst, Offenbach/Main)

[2] Gedeonov, A D , *Glav geofiz Obs* , **211**, 68 (1967)

[3] *Inadvertent Climate Modification* (*Report of the Study of Man's Impact on Climate*) (MIT, Cambridge, Mass, 1971)

[4] *Man's Impact on the Climate* (edit by Matthews, W H , Kellogg, W W , and Robinson, G D) (MIT, Cambridge, Mass, 1971)

[5] Kukla, G J , and Matthews, R K , *Science, N Y* , **178**, 190 (1972)

Thermal Plumes in the Earth's Mantle

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Dr Tozer casts a critical eye over the concept of thermal plumes that is attracting a good deal of attention in the Earth sciences just now.

IN spite of declarations of belief by distinguished geophysicists at a recent Royal Astronomical Society meeting devoted to this subject that thermal plumes do not exist in the mantle[1], the matter seems to be of sufficient current scientific interest to merit a less theological treatment, and with this in mind I have been asked for my comments as an interested spectator.

I do not propose to waste more than the minimum of space on the question of the existence of thermal plumes, for the answer seems to depend on the way one chooses to use language. Besides, physical scientists are generally more interested in the usefulness of a concept rather than in any philosophical discussion of its reality or existence. When a geologist, at least the species that exists in the minds of physicists, if nowhere else, uses a technical term he seems to do so as a name for which the question of existence is a pure tautology. In particular there is no reason to think that the words "thermal plume" are now being used by them in any other than this sense to name collectively such diverse phenomena, inferences and ideas as, for example, that abnormally hot material rises from the bowels of the Earth to escape in the structures we call volcanoes, the process that produced the Hawaiian Islands, the pseudo-elastic structure of the deep interior of the Earth is not spherically symmetrical. As nobody has enumerated the criteria that have to be satisfied for inclusion under this particular name and, moreover, because in many minds such inclusion has come to be seen as an explanation of mysterious events, the number of "thermal plumes" shows the same tendency to increase with time as was shown in earlier epochs by "witches", "layers in the crust", "tectonic plates", and so on—my geological friends assure me that several tens if not hundreds of "thermal plumes" have now been discovered. One cannot deny on logical grounds this or any other attempt to classify geological phenomena, although on the grounds of previous usage, I think one can justifiably object to the nomenclature in this instance. I hope it is clear that a scheme to associate events or phenomena is no more a scientific explanation of their occurrence than is the fitting of a curve to a selection of experimental points, unless there is also a definite proposal as to the procedure by which it might be refuted.

Question of Definition

I suspect that the rather loose usage of the term "thermal plume" sprang from a desire to have an original theory that would seem to make more immediate contact with geological observations than thermal convection theory, and an unwarranted eagerness to dismiss thermal convection as the theory that only predicted velocity fields in the mantle that were as smooth and symmetrical as they were geologically unacceptable. But there is no doubt that in its original meaning the term "thermal plume" did refer to convective flows—in a recent review by Turner[2] buoyant plumes and thermals are described as "a variety of phenomena related under the heading of turbulent buoyant convection from small sources" and in particular "a plume arises when buoyancy is supplied continuously". As a definition this description, with its tacit reference to plumes as flows of high Reynolds number, is too restrictive, I believe, to capture what one would like to express by the term "thermal plume" and at the same time too vague to decide whether dynamically similar flows might occur in the Earth's mantle. If one did take it as the definition, the fact that most authorities estimate the Reynolds number of mantle flows to be $\sim 10^{-20}$ could be taken as a clear judgment that thermal plumes are not a useful concept in this context. Perhaps a definition of thermal plumes which comes closer to expressing one's intuitive meaning is that it is a way in which one describes a thermal convective flow in which a velocity-dependent length, usually referred to as the thermal boundary layer thickness, is small compared with the linear dimensions of the system. This may be shown to be a convective flow for which the Péclet number $Pe = vL/K \gg 1$ where v is a characteristic speed of flow, K the thermal diffusivity of the medium and L the linear dimensions of the system. Taking from geophysical observation $v = 10^{-7}$ cm s^{-1} (3 cm yr^{-1}), $K = 10^{-2}$ cm^2 s^{-1} and $L = 10^8$ cm, we get $Pe \sim 10^3$, which certainly satisfies our condition. One could still raise the objection, however, that this is only a necessary condition for the existence of thermal plumes and that the flow would not, for the following reasons, match the "thermal plumes" envisaged in the mantle (see, for example, ref. 3). In the first place, one notices that the Prandtl number, $Pr, (= \nu/K)$ of mantle material is universally believed to be enormous ($\sim 10^{22}$) and, as $Pr^{\frac{1}{2}}$ gives the ratio of thicknesses of the viscous and thermal boundary layers, one sees that no large velocity gradients would be expected to exist at the limits of any attached or detached thermal boundary layer—a feature that has been taken to be characteristic of thermal plumes, and which is fairly clearly exhibited by high Péclet number flows in the atmosphere and ocean where the Prandtl number is 0.7 and ~ 7.0 respectively. Incidentally, the fact that a purely formal calculation of viscous boundary layer thickness in the mantle gives a length greatly exceeding the dimensions of the mantle would seem to belie some rather mystical talk that one part of the mantle is "decoupled" from another, but perhaps someone else could explain what is meant by that.

The second objection to thinking that the high Péclet number calculated here is sufficient reason for believing that the deep mantle has ascending plumes of hot material is based on an estimation of the thermal energy flowing into the mantle from the core. It will be recalled that one of the persistent difficulties of geomagnetic dynamo theory has been to find a source of energy that will sustain the necessary motions and at the same time be acceptable to geochemists. Translated into terms that are relevant to the present problem, one can call this the difficulty of supposing that less than $\sim 90\%$ of the heat flowing through the Earth's external surface has been generated throughout the mantle/crust region. Although there has recently been some change of attitude among geochemists about the possible potassium content of the core, it is still hard to believe that the mantle/crust system has anything like as much heat entering at the bottom as is measurably leaving it at the external surface, and it is because of this difference in the spatial distributions of heat supplied and lost that one must expect the concept of a plume as a detached thermal boundary layer to be more descriptive of cold descending material near the external surface than of rising material This asymmetry of the flow in comparable circumstances of volume heating and surface cooling has now been clearly demonstrated in model experiments[4] Of course, the more one is prepared to confine convective motions, such as by rapid change of rheology with radial distance, to the outer parts of the mantle/crust system, the easier it is to justify a significant heating from below and a description of that motion in terms of both rising and falling streams containing thermal boundary layers But the extremely large Prandtl number of the situation should warn one that the rising stream is no ordinary thermal plume, and it is obvious that such a more or less upper mantle flow cannot match all the attributes ascribed to "mantle plumes" by geologists

From these remarks, it will be seen that a decision to use the words "thermal plume" to describe only those convective flows that are dynamically similar to certain observed flow phenomena that have been named thermal plumes in the atmosphere and ocean leads to the conclusion that they do not exist in the mantle/crust material This may be the source of some misunderstanding Although some geophysicists may quite justifiably feel that lack of dynamical similarity is sufficient reason to ban the words in a geotectonic context, they have not been clear enough in their own minds to point out that a mantle flow which locally has a reasonably close but purely kinematic similarity to atmospheric thermal plumes is still not denied by mantle convection theory In fact, as I have spent some years in advocating that in the most plausible formulations of the mantle convection problem very narrow columns of rising and abnormally hot material can be expected as part of the general circulation, I should like to describe briefly this view of the convection problem because it may help to define our subject matter and establish contact with general geophysical theory

Two Factors

In a study of the Earth's response, and indeed that of the other planets, to any geochemically plausible distribution of heat sources, one is compelled to include *ab initio* the variation of material rheology with temperature and the production of heat during any material deformation These two factors are present, of course, in all the well studied laboratory systems, the atmosphere and oceans, but it transpires that they have no great significance for the understanding of those systems, save in certain very restricted circumstances where the lifting of a degeneracy that would otherwise exist is of prime observational interest They can be added to a theory that initially ignores them as a kind of afterthought In contrast, with planetary problems the numerical value of the constitutive function representing the material rheology is very strongly influenced by the flow itself, rather than just by the boundary conditions This adds to the complication of making a precise theoretical analysis and destroys the possibility of close dynamical similarity with any other system differing much in size Limited calculation has already shown that the response of a planet to its heat sources is quite different from what has been expected from certain oversimplified methods of analysis, for example, by studying it as a problem in heat conduction theory or as equivalent to heat transfer in a body with a particular temperature-independent rheology The salient results of the efforts to elucidate the steady state response for a set of planetary models that would cover the wide range of possible planetary materials can perhaps be best summarized in the language of control theory One finds that the heat transfer process acts as a powerful negative feedback to keep the horizontally averaged numerical value of the rheology function below a certain depth (expressed purely dimensionally in units of viscosity) nearly independent of its particular dependence on temperature

Further indication of the strength of this feedback is shown by calculations of the rapidity with which a postulated non-steady state situation relaxes to the steady state This turns out to be typically of the order of a few hundred million years, though the non-linearity of the problem makes it not always possible to characterize relaxation from an arbitrary initial state quite this simply The situation in the Earth is further complicated by the influence of hydrostatic pressure on the rheology, but calculation showed quite clearly that the average "viscosity" below a depth of a few tens of kilometres and above a few hundred kilometres would be tightly constrained to be about 10^{20} to 10^{21} poise (ref 5) Although this particular figure and other predictions of the steady state solutions give a quantitative interpretation and coherence to a wide set of terrestrial observations, such a strong constraint on upper mantle rheology seems at first to make the existence of magma, that is, material with "viscosity" at least 10^{14} times less than the figure just mentioned and the *sine qua non* of geologists' "thermal plumes" (?), even more problematical than with the earlier theories of a planet's response to its heat sources

Magma Formation

Ever since Lord Kelvin showed that the Earth as a whole has a higher rigidity at tidal frequencies than that of steel at room temperature, scientists who have tried to answer the problem of magma formation can be broadly grouped into two classes In the first were those anxious to preserve a spherically symmetric view of the Earth's interior who were forced to assert that Earth material could exist in a state that simultaneously combined the requisite rigidity and viscosity, whereas the others saw magma generation purely as the result of some local anomaly in material composition I believe a less *ad hoc* explanation of magmatism that makes it a part of the overall global response has now been found in an interplay of viscous dissipation of the internal motions and the decrease of "viscosity" with a rise of temperature It may be shown that the ratio of the heat produced by the viscous dissipation of a motion to a "primary" heating that is assumed responsible for the existence of that motion increases with the size of a system and approaches 10^{-1} in a typical planetary situation A value of $\sim 10^{-8}$ in any practical thermal convection experiment ensures that the interplay referred to never leads to any observable consequences there, but I believe it is possible to make some safe conjectures about the results of scaling upwards in size at fixed Rayleigh number, the empirical configuration that at the moment seems the closest simulation of a planetary situation—I refer to an internally heated plane layer with Rayleigh number $\sim 10^6$ and Prandtl number $\sim 10^2$ that is cooled from above and thermally insulated below One can expect that because any plausible planetary "viscosity" function decreases in value with increasing temperature, the spatial inhomogeneities that are present in the rate of shear field on a laboratory scale become both more enhanced and concentrated as the depth of the layer is increased As it is now known that on a laboratory scale the average rate of shear throughout descending material in internally heated flows at such Rayleigh numbers is much higher than elsewhere[4], one expects the effect of viscous dissipation in reducing the "viscosity" and sharpening the peaks of the rate of shear distribution to be first manifest there, and that there would be some concomitant redistribution of the heat flow at the upper surface that relatively enhances its value over descending material It is possible to show that for layers whose depth exceeds about 10 km and those average viscosity is $\sim 10^{20}$ poise, the shearing within the descending material would have evolved to a type of quasi-discontinuous slip across a zone that is extremely narrow compared with the depth and which contains material with a "viscosity" that is typical of magma (with all that that implies about a temperature anomaly) One senses that such zones might well grow out of relatively small inhomogeneities of a flow that was at least on the scale of the upper mantle, but the asymmetry of the situation that is due to volume heating and surface cooling leads to the prediction, probably the most characteristic of this theory, that magma production is principally associated with descending material

It is unfortunate that the purely technical difficulties of handling a problem that involves such a wide range of length scales have precluded a more detailed development of this theory of magmatism, but among its most attractive features that seem to match observation and which should be sufficient bait for any intrepid theoretician are (1) A natural explanation of the non-random distribution of volcanoes and their positional correlation with descending material (2) A resolution of the rigidity-cum-viscosity paradox by the prediction that almost all upper mantle material is constrained by the heat transfer process to have a viscosity $\sim 10^{20}$ poise, and that the thermal/rheological condition of matter that we call magma can only obtain in extremely narrow zones "thermal plumes" (3) The rate at which the total viscous dissipation can produce magma, that is, reduce the viscosity of mantle material from $\sim 10^{20}$ to $\sim 10^{6}$ poise, is a few cubic kilometres annually—a figure that has also been estimated from geological observation

I would like to think that such figures for the total magma production rate would have a calming influence on the much publicized problem of the site of the Hawaiian Islands It will be recalled that their location at the centre of what has come to be known as "a rigid plate" has caused much consternation, though I cannot help thinking that this problem is rather like that of a man who insists that the Earth is flat, and who is constantly perturbed by the disappearance of ships over his horizon The volume of material that comprises the Hawaiian Islands is indisputably enormous to the human mind, but represents an exceedingly small fraction ($\sim$0 1%) of the magma that would have been produced in the period of their formation and existence I cannot think of any other problem involving finite deformation theory where failure to account for the disposition of such small fractions of a total mass flux is regarded as a theoretical failure or indeed of such scientific importance

New or Old?

Having accepted the invitation to write an article that was supposed to comment on the theoretical respectability or otherwise of thermal plumes in the mantle, I have found it extremely difficult to decide whether theoretical geophysics was being asked to comment on a new phenomenon or on the current jargon for the very old and real problem of magma production One has been constantly in the position of having to define what others mean by the title in order to make intelligible comment and I am very conscious that, in trying to do so, I may well have knocked down or elevated my own Aunt Sallys My fears in this respect were not helped by a recent editorial in *Nature*[6], which commented that some phenomena that had been attributed to "thermal plumes" might well prove explicable in more conventional geological terms It would be most helpful if someone would explain in terms that are meaningful to geophysicists in what respects the conventional geological pictures of rising magma differ from "a thermal plume" I would wholeheartedly agree with P J S that "something is clearly going on" and that it is highly desirable to test alternative explanations of the data[6], but if that is to amount to more than a pious hope, the protagonists of "thermal plumes" have to stop using the words as a name for phenomena or states of mind—for example, "that which makes the situation around Iceland more complex"—and frame a definition that is amenable to test

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[2] Turner, J S, *Ann Revs Fluid Mech*, 1, 29 (1969)
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Applicability of Plate Tectonics to Pre-Mesozoic Time

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Plate tectonic theory has provided a synthesis to account for the geological development of the Earth's crust during the past 10% of its history. Doubts are now being expressed, however, about the applicability of this theory to the origin of some zones of deformed Precambrian rocks.

THE plate tectonic model[1] is, in the first instance, an instantaneous description of present-day crustal behaviour It is recognized that the crust and the top few tens of kilometres of the underlying mantle (together known as the lithosphere) behave as a small number of rigid plates in motion relative to each other and to the rotation axis of the Earth[1-4] Virtually all seismic, volcanic and tectonic activity is localized near the margins of these plates and is associated with differential motion between them The margins are of three kinds At extensional margins two adjacent plates are moving apart as new oceanic crust is created, in general accompanied by formation of an ocean ridge At convergent or destructive margins two adjacent plates are moving towards each other and motion is generally taken up by one plunging by subduction beneath the other Only oceanic parts of plates seem to be subducted to substantial depths When continental material is involved at the margin of the active plate it is generally deformed and retained near surface, and the process is orogeny rather than subduction At translational margins two plates slide past each other without creation or destruction of crust

Inspection of the young parts of the ocean floor suggests that this style of behaviour is not unprecedented Along a boundary between two given plates the conservative segments form a set of parallel arcs of small circles centred on a uniquely defined axis, but extensional segments are arcs of coaxial great circles—the axes of the two sets being ideally identical Relative motions at such margins can be described uniquely as a rotation vector about this axis, the poles of this axis are called tectonic rotation poles

Former alignments of extensional plate margins are determinable from the orientation of linear belts of oceanic crust of a given age within plates, in practice these are chiefly recognized from linear magnetic anomalies which again are arcs of great circles Past alignment of conservative plate margins is betrayed by the traces of extinct transform faults In oceanic crust these are recognized by offsets of magnetic anomalies or as fracture zones, in continental crust they may be exposed as large transcurrent faults, again they form arcs of small circles In principle the tectonic rotation poles and angles that describe the motion of all plates can be determined in relation to extensional and conservative plate margins only as far back in time as the oldest preserved ocean floor with each plate It is this limitation, together with the fact that destructive plate margins are not amenable to this precise kind of analysis[5], that in principle restricts complete plate tectonic solution for the Earth's crust to the time interval since the formation of the oldest ocean floor preserved in the existing ocean basins (about 200 million years)

The reality is less than ideal, even for this interval of time Seafloor spreading data are far from complete Tectonic rotation poles calculated by different methods at a given plate margin do not always agree and are in many cases imprecise These shortcomings are partially compensated by two factors (1) The aseismic continental margins mark the initial break that later developed into an oceanic ridge, and their best fit provides a good estimate of the initial relative positions of continents bordering the aseismic oceans The rotations involved in making these fits can be described by a single Euler pole and rotation angle (after Euler's theorem which describes the geometry of displacement)[6] The Euler parameters are the vector sum of the tectonic rotations which, if known, would define the actual paths of relative motion in detail (2) From the additive property of related Euler or tectonic rotations, motion between two plates separated by a destructive plate margin can be determined indirectly provided a route can be plotted between them which crosses only extensional and/or conservative margins These analyses have *inter alia* enabled the relative positions of all continents to be plotted with reasonable though variable degrees of precision back to 200 m y and led to a reassembly of the principal continental fragments into a single continental mass Pangaea at that time (late Triassic) Because there are no indications of active plate margins of Triassic age within this reassembly, the analysis effectively takes one back to the beginning of the Mesozoic

Palaeozoic

For pre-Mesozoic time there are no data from the oceans of the kinds available subsequently, which is why "seafloor spreading" is excluded from the title of this article Current discussion of pre-Mesozoic continental drift is strongly reminiscent of the classical pre-1960s controversy about more recent drift, hinging on the interpretation of land-based geological and palaeogeophysical observations That classic controversy related principally to the geometrical fit of opposed continental margins, distribution of fossil floras and faunas, geographic continuity or discontinuity of crustal structures and other trends, and palaeomagnetism Together they were strongly suggestive of continental drift, but fell short of being utterly decisive Their partial failure, I suggest, derived from their undue reliance on facets of uniformitarianism which were, and remain, unproven—namely the permanence of modern-style climatic zonation to control organism distributions, and the permanence of the geocentric axial dipole character of the ancient geomagnetic field

The new controversy is being conducted on similar lines but without the assistance of geometrical fitting There are advantages of framing the problem in terms of the plate tectonic model even though that model cannot be tested as fully as it can for more recent time First, the climatic zonation model and geocentric axial dipole field model are now more securely based as a consequence of their compatibility with plate tectonic interpretations for the past 200 m y Second, plate margins are recognizable geologically by distinctive features for which one can search each interval of the older geological record, and the plates existing during each interval are characterized by lack of contemporary internal deformation (Much controversy, however, now hinges on whether these "distinctive" features are truly diagnostic as is often claimed, and as is discussed later in this article)

Extensional plate margins, where they develop into ocean ridges, naturally leave little mark on the continents Nevertheless their former presence may be suspected where pre-existing geological features are abruptly truncated (as, for example, on the west coast of Africa where orogenic belts and sedimentary basins are cut off at the continental margin, their former continuations now being found in eastern South America) Extensive flood basalts dating from the time of supposed rifting may be indicative, although they are not diagnostic Nascent extensional margins (of which the East African rift system could be a modern example[7]) may be recognizable within continents if their development was stifled before reaching the ocean ridge stage, they are then not indicative of large scale relative motion but are of interest as signs of the operative process

Conservative plate margins, transform faults, are suspected of being preserved as transcurrent faults on continents, but they seem to be rare Destructive plate margins are expected on the plate tectonic model to be preserved within continents, even if they initially developed in ocean basins[8,9] It is orogeny and related continental magmatism which is believed to be diagnostic, rather than the mere formation of thick geosynclinal sequences of sediments[10] If eugeosynclinal belts form at plate margins, then orogeny may follow immediately after deposition But miogeosynclinal (or miogeoclinal) sedimentary wedges may form within plates at an interface between a continent and an ocean and will not be deformed at a plate margin unless the spreading regime changes in that case there may be a substantial time lag between deposition and major deformation

Rocks of the ophiolite suite are now widely regarded as former ocean floor and their occurrence in orogenic belts is strong evidence of plate convergence But the severity of orogeny is such that little or no relics of ocean floor may outcrop, so that absence of ophiolites does not of itself deny convergence Occurrence of island-arc type volcanism may also be diagnostic, whether the same can be said of flysch or molasse facies sediments is less certain and it may be that these are not even diagnostic of continental margins, let alone plate boundaries Distribution of organisms may assist Palaeozoic continental drift interpretations where provinciality can be established, or where progressions of successively deeper water continental-edge faunal communities can be recognized[11]

The palaeomagnetic consequence of plate convergence is confluence of the polar paths for the individual plates, and their continuance as a common path after convergence has been completed This is analogous to the confluence of Phanerozoic polar paths for each continent towards the present poles on the present-day map, and is the converse of the divergence of late Mesozoic and younger polar paths on a map of Triassic Pangaea (Fig 1)

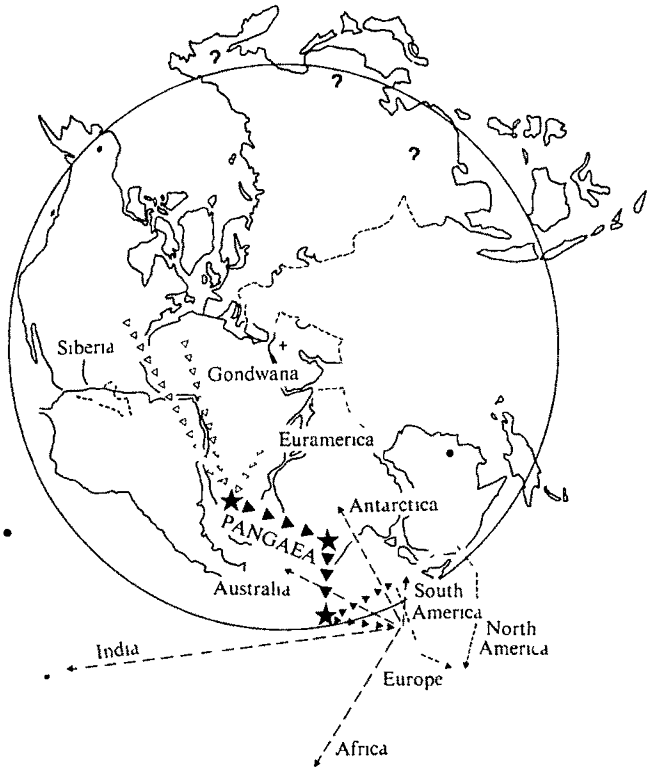

Fig 1 Stereographic map of the continents as they may have been situated at the beginning of the Mesozoic Palaeomagnetic polar paths are shown schematically Distinct early and middle Palaeozoic paths from Siberia, Europe–North America and Gondwanaland converge to a single late Palaeozoic/early Mesozoic track during which time this Pangaea reassembly may be correct The divergence of the tracks from later Mesozoic time reflects the dispersal of continents toward their present positions Slightly modified from ref 22

There are thus three independent suites of evidence which can be brought to bear on the subject of pre-Mesozoic continental drift—palaeontology/palaeobotany[12], "plate tectonic geology"[13], and palaeomagnetism To conduct the investigation in this fashion does not imply *a priori* acceptance of the plate tectonic model for pre-Mesozoic time, though it would be surprising if a style of behaviour which seems to have been universal for the past 200 m y were completely inoperative at any time previously This has not always been agreed[14], however, and as recently as 1970 Dietz and Holden[15] seem to have regarded "Wegenerian" drift as a unique event in Earth history On the other hand, 200 m y is less than 5% of the age of the Earth and the geological record within the continents stretches back to 3,000 m y (exceptionally to 3,400 or even 3,800 m y) and it would be equally indefensible to accept without question a ten or twenty-fold extrapolation of the model through time The desirability of determining the overall style of crustal behaviour for the duration of the entire geological record is self evident, whether or not the plate tectonic regime operated throughout in its latter day fashion may emerge from investigation

Palaeomagnetic and plate tectonic interpretations concur in the view that in the late Palaeozoic/early Mesozoic the continental crust was congregated principally in the single Pangaea group (Fig 1) There may, however, have been exceptions The most notable uncertainty relates to China, the age of whose juncture with Siberia is not very well established, but other peripheral slices of Asia, Australasia and elsewhere may also have been separate

That the Pangaea situation was ephemeral has been argued on general grounds by Holmes[16] and on specific geological[17,18] and palaeomagnetic evidence[19], all of which visualizes at least three continental groups in the earlier Palaeozoic[20–23] (Fig 1) That Siberia was one of these, having distinct geological and palaeomagnetic records before being sutured to Europe at the end of the Palaeozoic, has been argued by Hamilton[24] The Caledonian and northern Appalachian orogenic belts have been identified as the site of a "Proto-Atlantic ocean" between Europe and North America, with Greenland and the extreme north-western margins of the British Isles attached to the latter[17,25] but the palaeomagnetic evidence for this is not conclusive[26] The size and timing of the evolution and eventual disappearance of this Caledonian ocean remain uncertain Structural and volcanological arguments have been cited to show that it was wide in Ordovician time[25,27] and that oceanic crust still persisted in parts in the early Devonian, other chiefly petrological[28] and palaeomagnetic evidence, however, seems to indicate that it was already narrow by the mid-Ordovician and at the time of writing it remains plausible that Europe and North America were fairly close throughout the Palaeozoic That is why I have referred to a few "continental groups" rather than attempting to specify the number of early Palaeozoic continents The third of the three groups (after Siberia and Europe/North America and not knowing the whereabouts of China) seems to have been comprised of the Precambrian and Palaeozoic heartlands of South America, Africa, Antarctica, India and Australia assembled together and being cut by no orogenic belts younger than 500±50 m y This is essentially the Gondwanaland[29] recognized in terms of continental drift by du Toit[30] for late Palaeozoic and Mesozoic time The convergent plate margin(s) subsequently suturing it to North America and/or southern Europe probably lay within the Hercynian-Alleghenian orogenic belt, and various lines of suture within it have been suggested[31], but precise demarcation must await a better understanding of the Palaeozoic geological setting of southern Europe

Rates of polar shift determined from palaeomagnetism cannot be transposed into rates of crustal drift, without making assumptions about the relative positions of the plate and the Euler and palaeomagnetic poles There is rarely any evidence for these relationships although some limits may be definable if well defined segments of polar paths are found to form arcs of great or small circles It is possible that "quasi-static intervals"[32], when the palaeomagnetic pole seems to have been stationary, may be due to proximity of the Euler and palaeomagnetic poles to each other, rather than to cessation of plate motion Nevertheless the timing of polar shift can be equated with the time of maximum plate motion and it is interesting to note that in the examples so far investigated (Caledonides and Hercynides) this seems to predate the climax of orogeny by some tens of million years Hence it may be correct to distinguish an earlier phase of major plate motion and island-arc type orogeny, from a later phase (continental collision type orogeny) in which relative motion of the converging plates is relatively small The former is the more obvious palaeomagnetically and the latter is the more easily recognized geologically The apparent long duration of the later phase seems to indicate that continental collision does not put an immediate stop to convergent motion in the underlying asthenosphere

Thus hazy pictures are beginning to emerge of continent distribution back to 500 m y or so But that is still only seven or eight per cent of the whole geological record, there is still a long way to go, and progress becomes more difficult as the record becomes more and more fragmentary

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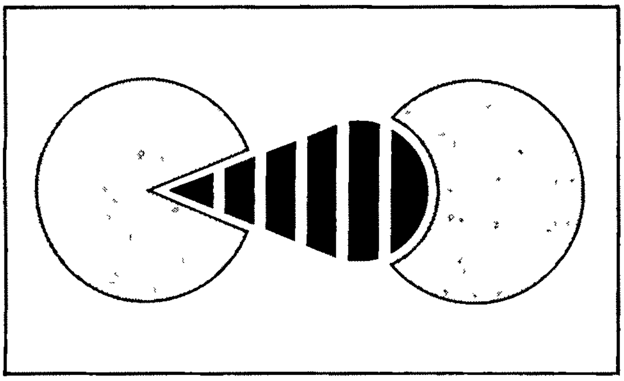

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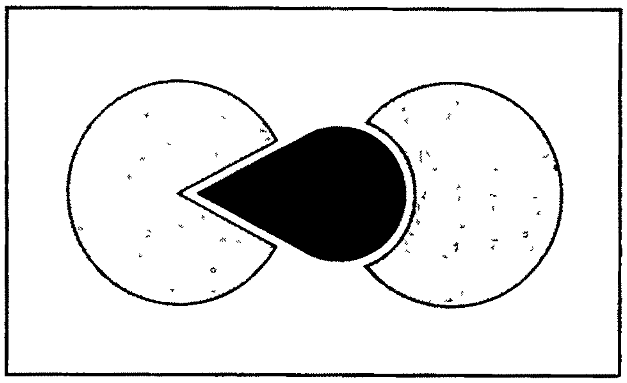

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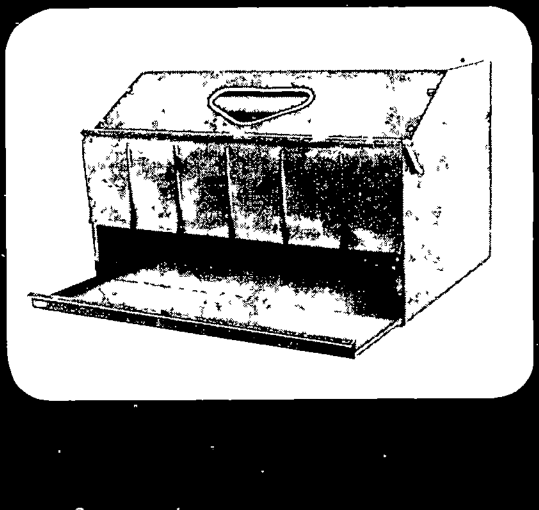

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Precambrian

Such evidence as there is for earlier time is principally confined to a few large regions of Precambrian crust which have been especially well studied Moreover the number of independent lines of evidence is reduced in default of widespread faunal occurrence The geological map abounds with older orogenic belts, each of which may be suspected as a convergent plate margin, and intervening stable cratons which remained undeformed during long periods when they may be regarded as plates in their own right

Burke and Dewey[33] have cited occurrences of tholeiitic and spilitic pillow lavas, cherts, andesitic and dacitic volcanics and ultrabasic rocks as evidence of destructive plate margin activity and large scale subduction of ocean floor during continental collision along various segments of the Pan-African and some older orogenic belts in Africa, and have inferred that this analogy can be extended elsewhere

Geochemical evidence of characteristic island arc-type processes is persuasive[33] and on this view reactivation of continental crust in these zones is ascribed to thickening of continental crust following collision, while the extraordinarily broad metamorphic belts adjacent to these zones are likened to the lower half of the thick Himalayan crust at the present time Although these arguments are at their weakest in defining the amount of convergence involved, Hurley[34] has rightly remarked that application of the modern plate tectonic analogy to the exceptionally long-lived orogenesis of many of the older belts requires enormous amounts of motion and the destruction of hemisphere-sized oceans

The contention of Holmes[35], Kennedy[36] and many others[37–39] that the Pan-African and older orogenic belts in Africa were essentially intracontinental stemmed principally from recognition that in some cases pre-existing geological features were not substantially offset by them, and that in others progressive correlation of facies and deformation phases was possible across entire belts (Interestingly most of these authors refer to "mobile belts" rather than "orogenic belts") On this model reactivation of older continental crust at orogeny is ascribed to exceptionally high subcrustal temperatures and the crust need not have been of abnormal thickness The finding that the supracrustal rocks are underlain by continental basement is not of itself convincing evidence of purely "intraplate" orogeny, although the preservation of relict areas of granulitic basement tends to support this view Moreover, preservation of relict oceanic crust is by no means assured in plate margin orogeny Realignment of pre-orogenic geology could be achieved if orogeny were always the culmination of a seafloor spreading/subduction cycle at the end of which the margins resumed their pre-spreading position[13] Some such reversibility in the spreading process seems to be implicit, for example, in the Proto-Atlantic ocean models[17,25], but there is no hint that controlling forces of the required kind have ever existed, indeed the finding in young ocean basins that tectonic rotation poles move quite substantially makes it inconceivable that the spreading path could be accurately retraced in any future convergent phase

Palaeomagnetism offers the prospect of resolving this evident impasse because, as Piper *et al*[40] have pointed out, the various tectonic hypotheses predict utterly distinct patterns of palaeomagnetic observations Palaeomagnetic field directions inferred from a single plate should be consistent with a single apparent polar wander path (polar path) relative to that plate Polar paths from plates in unrelated motion should differ drastically If a set of plates were loosely aggregated, predictable similarities and differences in their polar paths should be evident

Late Precambrian polar paths (for 1,000 m y onwards) from Africa and the Canadian Shield are utterly different, as would be expected if they were separate plates[41–43], and it may be that they had always been separate[41,42] Although mere similarity in size and shape of two contemporaneous polar paths does not prove that the two should be superimposed throughout their length, Piper[43] has demonstrated that if this is done for the time interval 1,400 to 1,000 m y it follows that the Canadian and African shields were adjacent during that time, and could have been parts of the same plate This is not to imply that plate tectonics was inoperative between 1,400 and 1,000 m y , such a conclusion would only be tenable if palaeomagnetic and geological evidence from *all* surviving crust of that age were compatible with aggregation in a single plate Indeed it is most improbable that that will prove to be the case, because it already seems clear that the Grenville province was converging towards the rest of the Canadian Shield during this same period of time[44]

Alongside this evidence of relative plate motion at least 1,300 m y ago, the speculation by Piper[45] that several of the cratons of Africa were already in essentially their present relative positions by 2,200 m y is now supported by a wealth of new data[40] A simple part of this evidence is illustrated in Fig 2, in which palaeomagnetic poles derived from the Kaapvaal, Congo and West African cratons seem to fall on a common path Inevitably there are statistical uncertainties associated with each estimated pole, and the time coverage from individual cratons is incomplete Hence the polar path in Fig 2 is drawn as a swathe whose width gives some idea of the amount of relative motion between cratons that the data will tolerate (say, 1,500 km) It shows that the destruction of a Mediterranean-sized ocean is tolerable, but not one as large as the modern Atlantic, and it flatly eliminates the possibility that hemisphere-sized oceans have been destroyed between these cratons The same conclusions would be drawn if one looked at data for any interval of a few hundred million years Taken overall, the data for 2,200 m y to the present all conform to such a long and complex common polar path that even 1,500 km is likely to be a gross exaggeration of the amount of distortion The implication is that Africa has been a single continent since at least 2,200 m y because even the possibility of "reversible" plate motions (opening and then closing an ocean so that the margins resume their original fit) is eliminated unless the reversibility was immaculate to a degree which is hard to credit

It may be contended that the palaeomagnetic data and the evidence of structural continuity are still inadequate to prove

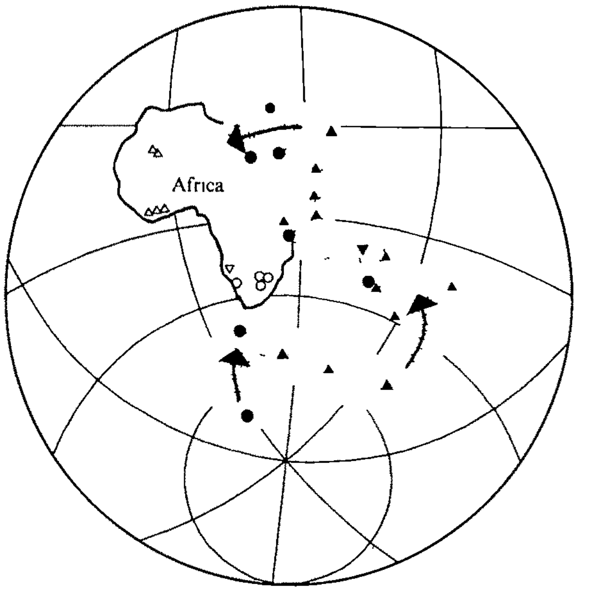

Fig. 2 Stereographic map of palaeomagnetic sampling areas (open symbols) and pole positions (solid symbols) from African rocks in the approximate age range 2,300 to 1,950 m y Kaapvaal craton, circles, Congo craton, inverted triangle, West African craton, upright triangles The small symbols imply that poles were calculated from measurements at single localities only, large symbols denote the mean from several localities Modified from ref 40

that the orogenic belts under discussion formed entirely *in situ* within a pre-existing continent But the case is sufficiently strong to justify questioning the extreme plate tectonic view that the occurrence of orogeny necessarily implies that large areas of ocean floor have previously been subducted on its site, and in the remainder of this article a number of alternative origins and mechanisms will be entertained I would emphasize, however, that the converse proposition that destructive plate margins are only preserved in orogenic belts is not being queried here and also that it is merely a matter of taste whether one regards deformation within a continent as consistent with identifying that continent as a "plate" I am, therefore, not deeply concerned whether the following propositions are regarded as alternatives, or supplements, or merely aspects of plate tectonics as presently conceived

First, it could be suggested that the old mobile belts do have modern equivalents, but that none are exposed, being in the lower crust The distinction between Precambrian cratons and mobile belts would then be merely in level of exposure

Second, internal deformation of continental crust might have been more common in the Precambrian than since This proposition has a number of variants Perhaps Precambrian continental lithosphere was weaker because it was thinner The sharper gradients of temperature-sensitive metamorphic zones as found in Archaean rocks would support this view, but it is doubtful whether this state of affairs persisted as late as 550 m y and in any case it is doubtful whether the lithosphere could have been thin enough to buckle under the forces operating on modern plates

Perhaps it was weaker because it was hotter The occurrence of extensive volcanicity and plutonic magmatism within present crustal plates is currently being ascribed to localized thermal highs[46,47] Whether these are to be identified with plumes of exceptionally hot mantle material is not critical in the present context What is noteworthy is that the proponents of Precambrian intracontinental orogeny, metamorphism and magmatism have invoked a similar cause Adopting for a moment the mantle plume picture, it is being suggested that the plumes migrate linearly with respect to the overlying lithosphere and hence might be capable of producing linear belts The precision of dating radiometric events within these belts has not been sufficiently precise to detect the lengthwise age variation which is implied in this model, but this is certainly within the capability of current methods Although this model may be capable of producing the actual metamorphism and magmatism it remains to be seen whether it can be reconciled with the compressive crustal pattern required to produce the regional orogenic deformation

Perhaps weaker parts of continental lithosphere deformed as a repercussion of continental collision elsewhere at a plate margin, however distant Such repercussions might take a long time to dissipate themselves, and the braking effects normally supposed to operate after continental collision at a plate margin may not apply

Perhaps convergent motion in the asthenosphere could be maintained for long periods, or even initiated, beneath continental lithosphere, despite the absence of modern examples After all, it is implicit in plate theory that divergent asthenosphere motions can be established beneath continental lithosphere and, until rupture actually occurs, must be decoupled from it Likewise after the initial contact of two colliding continental margins, convergent motion in the underlying asthenosphere must be at least partially decoupled unless subsequent phases of orogeny exclusively take up the inertia of the system

All these alternatives, and probably others, would be compatible with the long deformation histories of some Precambrian mobile belts, and, most important, for their observed superposition and cross-cutting relationships Given small amounts of relative motion they might also be compatible with the limited occurrence of volcanic and ultrabasic rocks otherwise associated with convergent plate margins

In conclusion it is worth repeating that the palaeomagnetic evidence which largely stimulated the latter part of this discussion does not contradict the hypothesis of plate behaviour of the crust On the contrary it strongly suggests that large areas of crust did behave as coherent units—perhaps rather too flexible to be called plates, but sufficiently rigid to maintain their shape and entity Clearly the investigation of pre-Mesozoic global tectonics is destined to pose problems for many years yet It seems at present that (contrary to experience for more recent geological times) palaeomagnetism will provide the more refined information, coming as it will chiefly from undeformed plate interiors The geological evidence, by contrast, is likely to be derived principally from deformed zones and for that very reason will be the more difficult to interpret The older palaeomagnetic data are, however, not expected to be superior to the younger, so that a picture of the behaviour of the Precambrian Earth as precise as that now evident for the Mesozoic and Cainozoic is not yet in prospect

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The Tempo of Human Evolution

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Dr Bishop here discusses the isotopic dating methods used in developing a time-scale for continental deposits yielding hominid and other mammalian fossils from the past 5 million years.

In the first programme of the BBC television series *The Ascent of Man*, the recovery of numerous hominid fossils from East Africa since 1959 was described by Dr J Bronowski as being "as exciting as the discoveries in physics before 1940 and those in biology since 1950"[1] Many of these finds were announced in *Nature* and have received wide coverage elsewhere Important as the discoveries certainly are, neither taxonomic arguments over that which we call *Homo* nor discussion concerning sophisticated reconstructions of palaeoenvironmental settings should obscure progress in a third field

This is the investigation of man's speed of "ascent". It calls for knowledge of rates of change in morphological characters of bone and tooth seen in the comparatively few specimens which successfully ran the gauntlet of scavenging by predators and breakage by weathering processes to become buried and fossilized Even fewer survive to be collected, or excavated, and take their place among that select band of fossils situated somewhere along the line which terminates in modern man The subject involves the establishment of a time-scale against which to view both the fossils and cultural evolution, as inferred from stratified lithic or other remnants of the litter so unthinkingly but usefully contributed by prehistoric men as indicators of the "tempo of cultural change"[2]

This review is written by a geologist "consumer" of isotopic dates rather than a specialist geochronologist In it I try to assess the progress and limitations of radiometric dating methods as applied to the past five million years (Pliocene plus Pleistocene) This is the time-span into which most of the new finds of hominid fossils and proven artefacts fall An understated but important feature of the recent East African discoveries is that they occur in mapped sequences of superimposed strata This permits fossils and artefacts to be placed immediately into a relative age sequence. Subsequently dates, and dating methods, can be checked against each other and subjected to the simple but effective judgment of satisfying the law of superposition Individual dated sequences for rich artefact- and hominid-bearing strata principally from the Omo Valley (Ethiopia), the Rudolf and Baringo Basins (Kenya) and Olduvai Gorge (Tanzania) combine to provide a time-base against which to view human evolution together with rates of change in other critical biological and physical parameters.

General Problems

Several problems beset those who would construct such time-scales, quite apart from technical difficulties associated with specific methods

(i) Continental and marine time scales Hominid fossils and artefacts are almost invariably preserved in continental environments Thus they have only a patchy distribution in space and time A reasonably complete record, and an inferred time-continuum, may be represented in carefully selected marine sequences and in the igneous substrate of persistently spreading ocean floors It is difficult to extrapolate dates from sea to land, however Conversely, most of the firmly dated horizons for use as time-lines in calibration of strata yielding fossil vertebrates have been established for volcanic rocks in well exposed, but incomplete, continental sequences Fortunately, palaeomagnetic stratigraphy, as described in more detail later, is proving a useful time-straddle between continental and marine sequences

(ii) Dating pedigrees The various unsuccessful attempts to date fossil bone have been reviewed recently[3] A reliable dating technique has yet to be established for fossil bones older than about 30,000 yr BP Radiocarbon dating has been applied with apparent consistency only to the collagen fraction of bones younger than 30,000 yr BP[3] Such dates would be given a pedigree of A1 under the system of grading suggested by Oakley[4] Some authors[5,6] have cautioned that fossil bones, like molluscs, are open systems and hence likely to give unreliable ages Although ages may seem to be valid they should not be accepted without careful scrutiny including stable isotope measurements and investigation of geochemical aspects of their sedimentary environments For bones older than 30,000 yr, an A1 pedigree, implying a direct determination on the specimen itself, is not yet possible For artefacts, the date at which they were made can be determined for specimens that have been accidentally heated in hearths, or by thermoluminescence dating of recent specimens Normally, however, a direct date on the specimen gives only the age of formation of minerals in the rock (or date of death of the wood) from which it was fashioned

Such considerations mean that most dates relating to hominid or artefact specimens occur in the lower grades (A2 to A4) on Oakley's scale[5] A statement outlining the stratigraphic relationship between the material to be dated and the fossil whose age is required should be recorded in the pedigree

Although the dating grades are largely self evident they are so frequently ignored that they deserve brief repetition. Many dates fall into an A2 category and are based on the age of some source deposit in which the fossil was found (such as potassium-argon ages on crystals from a primary ashfall stratifying contemporary hominids) A3 ages inferred by stratigraphic correlation from one locality yielding specimens to another where isotopic dates have been obtained are quoted frequently, however, without a qualifying pedigree

Finally, A4 grade ages, inferred by reference to some theoretical consideration, are commonly used but can be dangerous unless carefully qualified in the pedigree Palaeomagnetic reversals of polarity may be placed into this category but are proving useful where based on evidence from long successions for which detailed palaeomagnetic polarity studies, ideally with some isotopic dating control, have been carried out World-wide climatic changes recorded as stratigraphically recognizable events that are inferred to have time-significance may also be used (such as variations in palaeotemperature established by studies of foraminifera in deep sea cores or changes in tree pollen spectra of continental interglacial deposits) But such changes have the disadvantage that they are frequently time-transgressive

(iii) Climatic confusion. With care climatic data can be used in extrapolation to provide, at best, ages of grade A4 pedigrees It cannot be emphasized too strongly that inferred climatic cycles require calibration by isotopic dates to check firmly established stratigraphic data against such concepts as the Milankovitch hypothesis or similar theories of world-wide climatic change Climatic theory is not in itself a satisfactory basis for setting up a time-scale although it may assist in stratigraphic correlation Many workers hope that the Milankovitch or some similar hypothesis, based on correct prediction of periodicity of climatic change from knowledge of astronomical variables, can be developed into a dating method This may eventually prove to be the case but at present it is premature to use such an approach as the basis for a time-scale, as attempted recently by Evans[7].

Review of Methods

For more detailed information the reader should consult textbooks or reviews of dating methods based on quantification of the rate of decay of radioactive isotopes of carbon, potassium and uranium (radiometric "clocks")[4,8–10]. The brief outline and selected references given here for each method concentrate on recent advances and their relevance or limitation in relation to dating continental deposits through the past 5 m y

(a) Natural radiocarbon This method was put on a practical basis as long ago as 1949, following several years of research, and after recognition of its potential by Libby[11] Results are collated regularly in the journal *Radiocarbon* and revised details of techniques and problems are published from time to time[12] The range of the method is from the present to about 25,000 yr BP in general, but to 50,000 yr or more in ideal cases, for materials that have been in equilibrium with the carbon dioxide of the atmosphere Following refinement of the half-life of ^{14}C, recent research has concentrated on testing basic assumptions (1) that the rate of formation of ^{14}C is constant, (2) that ^{14}C is well admixed throughout the reservoir of atmosphere and biosphere, (3) that further ^{14}C is not added to the "closed" system after death of the organism which is the source of the dating sample The range of local variations in (2) can be monitored at the present day Variations of (1) with respect to time are of particular relevance to archaeologists[13], for, as shown by Stuiver and Suess[14], they upset the usually assumed relationship that one ^{14}C year is the equivalent of one year on the prehistoric calendar Correction curves, based on dendrochronology, comparing ^{14}C dates for the range 1,500 to 4,500 BC with "actual" age in tree ring years were published by Suess[15,16] and have been discussed by others[17] Recently Ottaway and Ottaway[18] have applied corrections from the Suess curve to various Neolithic cultures and draw attention to the need to take into account evidence from carefully excavated, well stratified sequences in addition to tree ring evidence in looking objectively at past changes in the concentration of atmospheric ^{14}C

Several workers[5,6] have stressed recently the need to minimize errors in dating young samples by establishing initial ^{14}C/^{12}C ratios But most errors in the application of radiocarbon dates to the stratigraphic record have arisen because of lack of recognition that the system to be dated is not closed[5], or from failure to collect specimens carefully in order to avoid contamination, particularly by young carbon in old samples For example, "modern" molluscs from Lake Edward in Uganda yielded ages of about 3,000 yr owing to the presence of old carbonate from calcareous volcanic ash after archaeological "dating" had suggested that radiocarbon ages for the Lake Edward Basin were too old Conversely, Page[19] recently published apparent ages well within the maximum range of radiocarbon dating for several peaty interglacial deposits in Britain Despite a pronounced clash with stratigraphic, geomorphological and archaeological evidence he ascribed a young age to the Hoxnian, its contained fauna and artefacts, and to other interglacials The most probable explanation, suggested by several lines of correlation with older dated sequences and supported by "infinite" ^{14}C dates on other specimens from the deposits sampled by Page[20], is contamination of the samples yielding the anomalously young ages by young carbon

These two examples emphasize the fact that not all materials have the same degree of reliability as potential dating samples. In order of increasing difficulty of determining the accuracy of the age, the best materials for dating are wood , grain, cloth, hides and so on , charcoal , bone collagen. Peat, dispersed organic matter and various forms of carbonate occur towards the end of the list.

Radiocarbon dating has contributed greatly towards a schedule of events through the past 50,000 yr (refs 21–23, for example) A different scale of accuracy applies when radiocarbon dates calibrate only the upper portions of cores and sequences A standard rate of operation of some process (usually deposition of sediment) is then used to extrapolate a time-scale without fixed points to periods before the past 50,000 yr This, however, applies principally to deep sea cores and to attempts to calibrate climatic change for periods spanning the early part of the last glaciation and the last interglacial By contrast, the histogram constructed by Isaac[2] draws attention to the fact that in continental deposits containing artefacts or hominid fossils there is a sharp "cutoff" of reliable isotopic dates at the threshold of radiocarbon dating Before this there is a hiatus of over one million years before potassium-argon dates become comparatively abundant and occur in long stratigraphic sequences

(b) Potassium-argon The decay of the radioactive isotope of potassium (^{40}K) with production of radiogenic argon (^{40}Ar) is widely used for dating rocks back to the age of the Earth During the past ten years it has been applied successfully to younger rocks in age ranges up to 1 m y and less One of the early applications to Quaternary strata was by the Berkeley Laboratory, University of California, in establishing an age for the skull of *Australopithecus (Zinjanthropus) boisei* from Olduvai Gorge[24,25]. The chief technical problems are in measuring the relatively small amounts of radiogenic argon that accumulate in young samples and in determining the fraction of ^{40}Ar that is of atmospheric origin In spite of these difficulties in dating young rocks the method potentially overlaps the older range of radiocarbon dating In practice, however, too few well substantiated dates fall into this time-span for the two methods to be checked against each other

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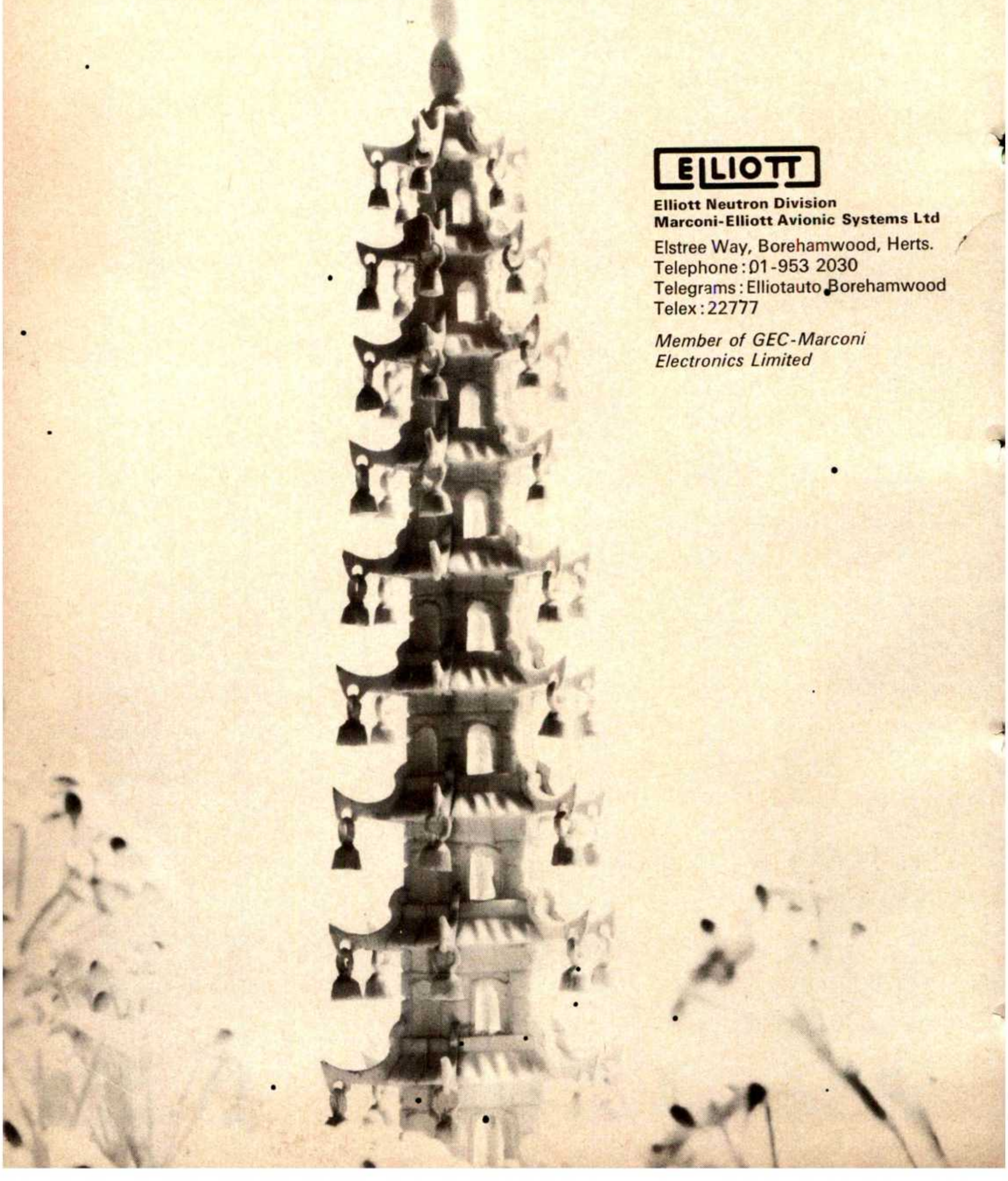

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Details are discussed in refs 26 and 27, and problems of contamination in ref 28 Recent developments of ^{40}Ar/^{39}Ar single sample dating and step-heating methods[29,30] are yielding more refined dates for the late Tertiary and Quaternary The ^{40}Ar/^{39}Ar approach offers a way of overcoming inaccuracies caused by sample inhomogeneity as it measures potassium content for the same sample on which the ^{40}Ar determination is eventually made This is in contrast to the conventional method.

Fitch[31] has reviewed the problems of assessing geological error and of selecting suitable dating samples Most likely sources of error again involve sampling of potassium-bearing minerals which are incorrectly assumed to be closed systems retaining all the radiogenic argon formed since the mineral crystallized Loss of some of the gas may arise through chemical weathering, physical strain or post-formational reheating of the rock All result in discrepantly young ages Inherited "excess" argon can cause discrepantly old ages but plotting of ^{40}Ar/^{36}Ar against ^{39}Ar/^{36}Ar isochrons offers a means of establishing the presence of excess ^{40}Ar and of possibly eliminating this problem[29]

Localities yielding potassium-rich rocks, or crystals, suitable for dating in clear and close relationships to artefacts and hominid fossils are limited In this respect the volcanics of the East African rift system and areas flanking it are particularly favoured Olduvai Gorge Bed I with 35 potassium-argon dates yielding a mean age of 1 82±0 13 m y. is the most accurately dated hominid-bearing unit beyond the range of ^{14}C dating[32] Some 100 feet of strata comprising Bed I and Lower Bed II in the eastern part of the Gorge were probably deposited in 130,000 yr or less[32] But no trend from older to younger is discernible in the dates for potassic minerals from tuffs through this thickness of strata. Although a sequence of fossils and artefacts can be derived from the known stratigraphic position of the finds[33] no rates of change can be established within the sequence because of lack of resolution of individual dates. This illustrates the need for caution to avoid placing undue weight on single or spasmodic potassium-argon dates.

Tuffs in the hominid-bearing Shungura Formation of the Omo Valley in southern Ethiopia have yielded a series of six dates for different horizons from 3 75 m y to 1 84 m y, all in correct order of superposition[34] A similar set of interrelated dates for the succession in the Baringo area of the Kenya rift, with its younger members yielding artefacts and hominids, can be checked against a long stratigraphic sequence, thus revealing any "misfit" ages[35] Fitch[31] has concluded that "successful potassium-argon dating requires scientific team-work and that isolated dates unrelated to a known regional chronology are unreliable" As more hominids and artefacts are excavated and the dating of these sequences is refined, rates of change should be discerned

(c) Geomagnetic reversals Although not in themselves a dating technique, changes in polarity of the Earth's magnetic field as recorded in both igneous and sedimentary rocks have proved extremely useful as a vehicle for extrapolating potassium-argon dates from well-dated into largely undated sequences

The development over the past ten years of the investigation of changes in the polarity of the Earth's magnetic field and their calibration by potassium-argon dating has been summarized by Dalrymple[36] This has resulted in a detailed geomagnetic reversal time-scale for the past 4 5 m y This period is subdivided into phases of normal and reversed magnetic polarity of which the major ones are termed epochs and shorter ones events[37] Rocks formed during times of reversal of the direction of the field, at epoch and event boundaries, have been located in both igneous and sedimentary rocks in marine and continental environments The resulting geomagnetic "time-scale" has been calibrated by almost two hundred ^{40}K/^{40}Ar dates which meet stringent requirements as to their accuracy

The method has important applications in providing a time-scale for continuous sequences in deep sea cores and in assessing comparative "rates" of seafloor spreading It also has the advantage that "refined" dates for reversal boundaries can be applied to incomplete continental successions providing that the typical "fingerprint" of a portion of the geomagnetic reversal scale can be recognized, preferably with confirmatory potassium-argon dating to help identify with certainty a particular reversal boundary or boundaries For instance, this has proved useful in correlation between Olduvai Gorge, the type area of the Olduvai Normal Palaeomagnetic Event, and other sequences As more palaeomagnetic studies are carried out on the fossiliferous lacustrine sediments of the East Rudolf area (and also other parts of the Kenya Rift) a pattern of epochs and events within the geomagnetic time-scale is being recognized This supplements the potassium-argon determinations in dating important hominid and artefact finds[38–40]

(d) Uranium series Methods based on the radioactive daughter products of uranium have been put to extensive use in dating only recently and the problems are not yet as well understood as for ^{14}C Three methods have been applied Decay of ^{231}Pa–^{230}Th has a range from 0 to 300,000 yr and is applicable only to marine sediments The relationships of ^{234}U–^{231}Pa–^{230}Th have a range of 0 to 150,000 yr or in some cases a little older Helium-uranium dating of corals raises several problems but seems reliable in the range 0 to 100,000 yr[6] The materials suitable for the methods are coral (unrecrystallized and cleaned aragonite), evaporites and volcanic rocks containing uranium , clean unaltered inorganic carbonates (tufas, travertines, oolites)

Mollusca, bones and other fossils are often rendered unsuitable because of alteration In view of the age limitations and the fact that coral is so far the only material which has been extensively tested, the method has only indirect application to continental environments Nevertheless, a date has been published for fossil bone samples from the Isimila Acheulian locality, Tanzania[41] If the method can indeed give meaningful results for continental deposits in the time-span older than 50,000 yr this could be a most important development Worries remain concerning the "open" nature of bone systems, however

The problems of radiometrically dating the episodes of high sea level and shorelines of last interglacial age, and also deposits of deep-sea cores assigned to the same period on palaeotemperature evidence, have been discussed by Shackleton[42] following work by various authors (refs 43 and 44, for example) Most of this sea-level evidence depends for calibration on uranium series dates on coral and oolite If a firm pattern of dates could be established for the last interglacial there would be the possibility of a link with continental deposits assigned on palaeoclimatic evidence to this period But reservations expressed by Thurber, Broecker, Bender[5,6] and others who have undertaken this research and the conclusions of Shackleton[45] suggest that firm isotopic dating is not yet available for marine successions of last interglacial age Shackleton[45] further comments that "many terrestrial Pleistocene deposits are ascribed to well-known named stages on the basis of an inadequate model" and thus he is "loth to comment on age determinations which are construed as dating these stages"

From a consideration of the radiometric data for the age of palaeotemperature peak 5e in the deep sea cores, Shackleton[42] suggests that it lies between 100,000 and 130,000 yr BP He concludes that the radiometric dates "do not show sufficient agreement to distinguish between the possible ages predicted" by various versions of the Milankovitch hypothesis and that "Workers interested in using the Milankovitch hypothesis as a framework for dating events further back in the Pleistocene can draw no comfort from the ease with which the hypothesis may be modified"[42]

(e) Fission track The techniques and problems associated with this method have been summarized recently by Fleischer and Hart[46] The method depends on the detection in minerals and glasses of trails of intense damage following fission of a uranium nucleus As the major isotope of uranium (^{238}U) decays at a slow and steady rate it is only necessary to establish the fraction of uranium atoms that have fissioned within a given sample in order to compute its age The age range of the method is from 20 to 5×10^9 yr and so it has potential as a means of cross-checking the results of several isotopic methods already described Indeed it was used successfully as a broad check on the initial potassium-argon ages established for Bed I at Olduvai Gorge[47] and has also been used at various recent archaeological sites and to date falls of tectites Materials that can be dated include uranium-rich accessory minerals (apatite, zircon, sphene, and so on) from tuffs, igneous or metamorphic rocks Obsidian, pumice and heated rocks or archaeological implements can be dated to determine their time of heating Study of the tracks is made possible by etching out the lines of damage and a large variety of etchants has been used[46] The method has application to the past 5 m y but more data are now required to broaden the coverage

Cerberus—the Dating Dog

Having reviewed the methods that have contributed dates relevant to the calibration of a time-scale for human evolution, it is important to stress the necessity of synthesizing information which for convenience may have been gathered and processed under the separate heads of chronometry, stratigraphy and biometry. The central need for sound stratigraphic control makes it possible to portray geochronology by reference to "Cerberus", the mythical three-headed dog (Table 1).

The principal subdivisions are summarized under the three heads and it is a basic requirement that Cerberus should have a pedigree (A1 to A4 as detailed above) in common with all other dogs. It is essential for information to be fed through and exchanged between any of the three heads. Finally, it is not entirely frivolous to add that although a climatic "tail" may occasionally have its part to play in maintaining the wellbeing of the whole animal it should never be allowed to "wag the dating dog"

Time-scales—Long and Short

Evans[7] has recently used climatic cycles as if their duration was reliably established and each could with certainty be related to observed features in the stratigraphic column He derived a time-scale based on twenty-five alternately warm and cold cycles each averaging 40,000 yr duration commencing from the "Calabrian" dated at 1 m y ago In a summary chart significant "radiometric dates tied to climatic phases" are related to "insolation and climatic cycles" and also to river terrace heights in Britain, to Mediterranean high sea levels, to magnetic stratigraphy and to "approximate dates of cultures" and fossil hominid finds

This situation seems remarkably similar to that developed in East Africa some years ago when a theoretical climatic-stratigraphic sequence was in vogue In Evans's system twenty-five warm and cold "pigeon holes" have climatic and other events slotted into them In much the same way archaeological and geological data were placed into the pluvial and interpluvial compartments of what proved to be the East African "climatic straitjacket" Fortunately in East Africa theoretical climatic considerations have been rejected in favour of normal stratigraphic practice[48–50] Firm evidence of climatic parameters is now being calibrated by isotopic dates and a pattern of climatic change is gradually emerging[21,51]

Problems of calibrating even the last interglacial satisfactorily have already been touched on under (a) Recent work by Imbrie and Kipp[52] attempted to quantify climatological data for the late Pleistocene obtained from micropalaeontological investigation of deep sea cores No simple "fit" with astronomically predicted climatic change was found But if such an approach can be combined with rigorous calibration and extended to many more cores it should enable the validity of climatic hypotheses to be fully tested

Dating glacial tills for periods before 2 0 m y has been successfully undertaken in the Sierra Nevada of North America[53], in Southern Argentina[54] and elsewhere, by combined application of potassium-argon dating and palaeomagnetic studies Again a broad pattern of climatic rhythm seems likely to emerge as more dates accumulate

For marine successions it has been fashionable to talk of "short" and "long" chronologies Cooke has set out the details of each and the problems of reconciling them[55] The "short" scale originated from oxygen-isotope curves constructed by Emiliani[56], is calibrated by extrapolation beyond the range of ^{14}C dates by reference to sedimentation rates, receives some support from uranium-series dates for the last interglacial, and has been extended to European continental sequences

The "long" scale was introduced by Ericson, Ewing and Wollin[57], has been modified by various workers as summarized by Berggren[58], is largely in accord with the geomagnetic polarity scale, and allows correlation with continental deposits in East Africa calibrated by $^{40}K/^{40}Ar$ for the age range from 1 to 3 0 m y and older

As far as the hominid record is concerned a longer scale seems to be demanded as artefacts and fossils from well-dated contexts range back through 2 0 m y to beyond 2 6 m y This seems impossible to reconcile with short scales where Acheulian or bifacial artefacts only range back to about 350,000 yr

In fact there remain many gaps in the evidence The South African caves containing australopithecine-bearing breccias together with the Choukoutien caves which yielded the Pekin *Homo erectus* material are undated by isotopic methods The *Homo erectus* open sites in Java have some

Table 1 Cerberus, the Dating Dog*

CHRONOMETRIC	STRATIGRAPHIC	BIOMETRIC
ISOTOPIC DATES (+PALAEOMAGNETIC POLARITY) ~A1 to A4 grades of pedigree	LITHOLOGY GEOLOGICAL MAP SEQUENCE OF STRATA ~Depositional rates	FOSSILS ~Correlation ~Palaeoenvironment ~Evolutionary rates

* A feedback mechanism exchanges data between all three heads and the pedigree similarly reflects information from all sources

radiometric control[59] but lack the clearly mapped long sequences of strata and fossils of the Kenya rift localities Even in East Africa enormous blanks remain, particularly between about 1 5 m y and 50,000 yr BP, for which more fossil evidence has still to be found or isotopic dates have yet to be established[10] Judging from the abundant finds and dates recorded during the past ten years, rates of human evolution should be discernible during the next decade

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Future of Electron Microscopy in Biology

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Electron microscopy, at present a versatile tool in the study of biological systems, can benefit from advances in instrument technology and its application.

OF all the methods now available for studying matter through its interaction with radiation, electron microscopy is the most versatile and the least specific Nearly all the advanced techniques presently available require the presence of many identical units in the specimen These techniques are immensely important to modern chemistry, and, indeed, methods such as X-ray crystallography already play a vital part in molecular biology, but their applications to the highly complex and irregular structures encountered in biology must be limited Electron beam technology is, however, unique in providing useful information down to the molecular and atomic level about the most complex and random of structures. Hence special importance for biology A central theme of this paper is the assessment of how one may hope to increase the precision of the information that electron beam technology can provide about systems which by the standards of the physical sciences are highly intractable

A typical unicellular organism, less than 2 µm across, synthesizes many hundreds of compounds by a precisely regulated process, is able to replicate itself, and is capable of the genetic evolution and modification of these processes If one wanted a quick way of destroying that uniquely delicate mechanism there is probably no better tool than a flux of fast electrons Yet precise information can be obtained about a meticulously prepared biological specimen by exposing it to a beam of electrons which in one second would boil away many times its weight of water.

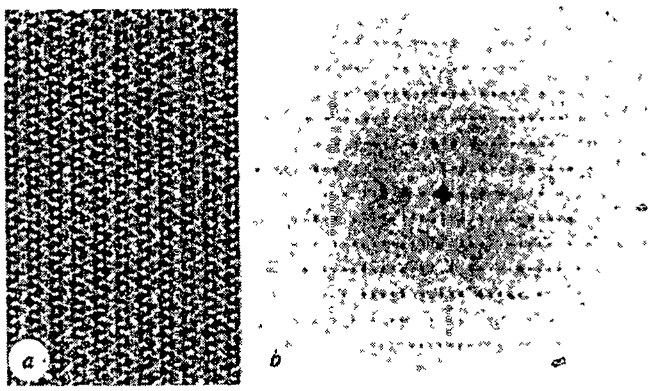

Fig. 1 *a*, Beef liver catalase (×175,000) treated with equimolar solutions of aluminium and uranyl formate and imaged over a hole in the substrate with a minimal electron dose. *b*, Optical diffraction pattern of the same area (1 cm=½ 25 nm^{-1}).

When electrons interact with matter they may pass through the specimen undisturbed, they may be elastically scattered by atomic nuclei with little loss of energy but with a wide spatial distribution, or they may interact with orbital electrons, being scattered with substantial transfer of energy but with small deflexion. Electron microscopy aims at interpreting and presenting as much as possible of the information about the morphology of the specimen which is carried by the scattered electrons. The consequences of the transfer of energy to the specimen are also of fundamental importance. Transitions of electrons between quantum levels may be accompanied by characteristic X radiation carrying analytical information. Electrons may be ejected with the formation of highly reactive species whose subsequent reactions change the chemical composition of the specimen, one of the most important causes of radiation damage. All such phenomena are inevitable consequences of exposing a specimen to high energy electrons, which initiates processes which can yield morphological and analytical information but also leads to reactions which alter its nature. The art of electron beam technology is to exploit these benefits while minimizing the deleterious effects.

Beam Technology and Biological Materials

The wavelength associated with a 100 kV beam of electrons is about 0.004 nm, so that the theoretical resolving power is far beyond what is needed to image any specimen, biological or mineral. In practice other limitations arise, and the lowest level at which one can get a reliable point-to-point image in the most favourable circumstance is about 0.3 nm. Strenuous (and costly) efforts are being made to achieve resolutions down to 0.1 nm, which, if there were no other problems, would permit the direct visualization of atoms in biological materials—perhaps the ultimate in ultrastructural investigations.

Instruments are now commercially available which can resolve distances of 0.5 nm or less. Direct visualization of biological material at this level would tell us much about the structure and mode of action of macromolecules and subcellular components such as contractile proteins and ribosomes, the nature of cellular interfaces, the ultrastructure of viruses, and about much else that can now only be inferred from biological and biophysical investigations, and is at present a matter of controversy and conjecture. Biologists would like to be able to work at these resolutions in circumstances where they can be sure that they are studying the specimens in their natural state. Unfortunately, serious problems stand in the way.

One of these, radiation damage, has already been briefly mentioned. As it invariably accompanies the process of observation, the object is to minimize it while at the same time getting as much information as possible. No biological specimen will remain entirely intact during observation: all one can hope for is to observe an entity which closely resembles the original specimen, and not a completely different artefact. In fact radiation damage can rarely be identified in biological specimens at resolutions higher than 1 nm, and it is a real possibility that deterioration may be virtually instantaneous, so it is to be hoped that the original structures survive substantially unchanged in the degraded product actually observed.

Although too little work has been done on the direct investigation of beam damage to biological specimens *in situ*, a good deal is known about radiation chemistry that is relevant to it. Much of this work has involved thin specimens, seeking model systems for the study of biological macromolecules among amino acids, polypeptides and carbon-chain synthetic polymers. Radiation damage appears to be diminished at low temperatures, perhaps due to the trapping or inactivation of radicals. It has been reported that damage results primarily from interaction with water in the residual gas in the instrument, though electron diffraction patterns of proteins have been obtained in environmental cells at a relative humidity of over 90%. There is a strong suggestion that high operating voltages favour survival: thus in one experiment using the high voltage electron microscope, damage to a crystalline synthetic polymer was found to decrease by a factor of 10 when the operating voltage increased from 50 kV to 1 MV. Supporting evidence has come from studies of amino acids between 100 kV and 2.5 MV.

To minimize radiation damage, as low a flux of electrons as will give an image unimpaired by statistical fluctuations in the beam must be used and there could be room for improvement in this direction in the practice of biological electron microscopy. Another approach, at present a matter of controversy, is the use of image intensifiers.

Other mechanisms of damage arise in the study of thick sections, particularly the knock-on effect by which an atom is ejected bodily from a molecule by an incident electron. If the specimen is sufficiently thick the displaced atom may be sufficiently energetic to displace another, and this sets up a chain of disruption until the initial input of energy is sufficiently dissipated. This effect becomes increasingly important above the threshold beam voltage above which an electron is sufficiently energetic to displace an atom (in the case of carbon, 30 kV). At still higher voltages (100 kV in the case of carbon) it begins to fall off again. It is another factor to be taken into account in determining the optimum conditions for operation.

Another problem, of comparable importance for the biologist to radiation damage, is that of obtaining adequate contrast in the specimen. The biologist is nearly always concerned with light elements of low scattering power. At the levels of resolution necessary for the study of cellular and subcellular particles, the most important method of increasing contrast is to observe not the specimen in the original condition but an object containing heavy metal atoms of high density. Three approaches to this have been evolved: (i) positive staining—the direct reaction of the specimen with heavy metal compounds, (ii) negative staining—replacing the hydrated regions of the specimen with electron dense material, (iii) shadowing—depositing an electron dense substance (usually a metal) onto the surface of a specimen at an oblique angle to accentuate its surface features. Some compromise is involved in all these methods, because to make the specimen visible it must be modified; here again, there is a danger of observing no more than an artefact. Specimen preparation is as important here as in other aspects of biological electron microscopy.

Staining is still largely an empirical procedure lagging behind development of instrumentation. Accurate methods are, however, being developed based on principles capable of wider application. In enzyme histochemistry our knowledge of

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the basis of reactions at specific substrate sites is comparatively well advanced. Uranyl acetate staining of DNA has been used to visualize aggregates of a few atoms in a strand about 3 nm thick. Very substantial rewards could come from the development of specific stains which can be applied so lightly that they do not appreciably modify the specimen—for instance the direct determination of the base sequence of DNA. The solution of such problems will demand all the resources of modern quantitative metal ligand theory. Negative staining may also be put on a more rational physicochemical foundation. The interaction between polyanionic species and biological specimens is found to be very sensitive to the condition of the aqueous medium, and unexpected analogies discovered between their solution chemistry and that of simple ionic species, which may contribute to our understanding of their action. Uranyl salts have been widely used as negative stains, but deteriorate during irradiation due to crystallization. Recent work has demonstrated the advantages of mixed systems over pure uranyl salts.

Investigation of Soft Tissues

What must be done before a soft tissue, consisting mostly of water, can be studied in a microscope? Most of the current methods for fixing and embedding are unspecific. Although they have proved more effective in preserving biological structures than might have been expected, they must also involve considerable distortion of the specimens, so inferential evidence from light microscopy, biochemistry and biophysics must be used to support observations. There is room for an organized physicochemical attack on these problems, but the best way of overcoming them is to avoid them altogether, for example, by so modifying the instruments that they observe the specimen in its natural environment—we return to this later. The alternative is to immobilize the water in the specimen by freezing.

The study of frozen tissues in the electron microscope is theoretically feasible, but formidably difficult in practice. Much modern work is concerned with developing and applying methods of very rapid cooling, which is essential because the ice crystals formed must be sufficiently small as not to interfere with the electron image, and because when the ice crystals are large, and an appreciable amount of solute is present, high local concentrations of ions can arise which might damage the specimen by osmotic shock. One method being developed operates at high pressures to give very small crystals at depths up to 200 µm in the absence of cryoprotective. In another, droplets of the specimen of diameter about 10 µm are sprayed onto liquid propane at −190° C. There has been considerable discussion as to whether truly vitrified water can be produced by the rapid freezing of specimens. This matter is still controversial.

The preparation and handling of frozen specimens present their own problems. If the specimen is warmed above the glass transition point of ice (−130° C) irruptive ice crystal growth may occur. Frozen tissues may be studied intact, but work with thin slices promises more. Ultracryomicrotomy is already an established technique, and several commercial instruments are available which can cut sections down to 20 to 40 nm. At present the lower limit attainable in usable sections is about 40 nm. To get thinner sections more needs to be known about the actual physical processes involved when cutting a frozen section with a microtome. The ideal temperature for section cutting is still doubtful. Ice crystal growth must be avoided, and we are still uncertain whether the process of cutting causes localized melting. Problems also arise in the transfer of the specimen. Devices are now being developed which avoid dehydration of the specimen, or its contamination by ice condensed from atmospheric vapour.

These difficulties apart, other problems arise with frozen sections. It is not yet certain that large quantities of water do not cause excessive electron scattering, with a consequent fall in signal/noise ratio, and it may prove necessary to compromise by removing free water from specimens for cryobiological study. It is not yet entirely certain that the electron beam does not cause melting: if it did, it would completely nullify the aims of the cryobiological approach. On the other hand, there may be incidental advantages. Radiation damage may be lower at cryobiological temperatures and cryobiology will certainly stimulate ultrahigh vacuum technology. Vacua better than 10^{-6} N m^{-2} (10^{-8} torr) will become increasingly important in reducing contamination in ultrahigh resolution freeze-etching studies, which aim to provide more information about the process of fracture in relation to the contours of the specimen.

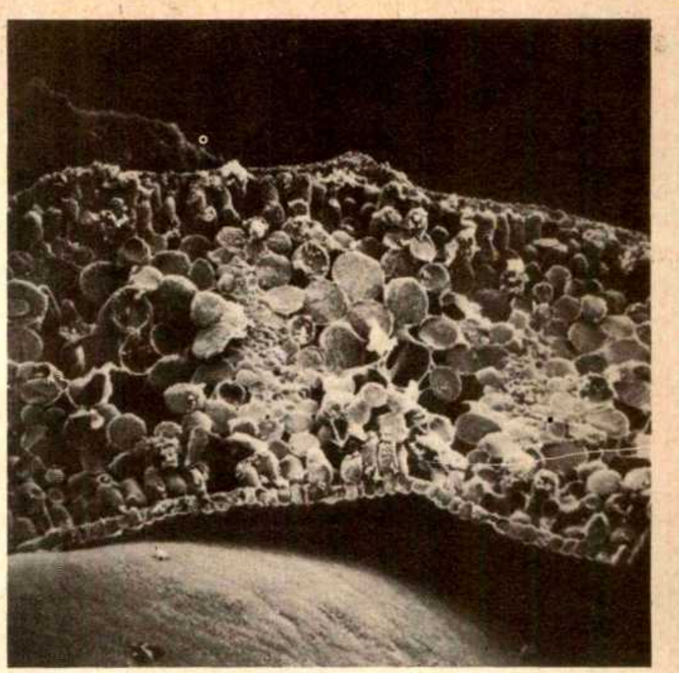

Fig. 2 Cryofractured *Muscari botryoides* leaf. The leaf was quench frozen in Freon 22 at −165° C and fractured under the cryogen. The specimen was then kept frost free at −130° C and coated with 15 nm of evaporated gold-palladium. The still-frozen leaf was transferred to the cold stage of a 'Stereoscan' S4 scanning microscope and photographed at −150° C at an accelerating voltage of 20 kV. Magnification ×200.

Environmental cells would avoid all these problems, but they introduce their own difficulties. In the past much emphasis has been placed on the preservation of vitality during exposure to the electron beam, but the comment that work in this direction "shows a healthy disregard for theoretical pessimism" seems well justified. Their use in the direct investigation of hydrated specimens is more promising, but also introduces its own problems, for the interaction of the electron beam with water vapour produces high energy ions which can be very destructive. Detailed investigations will be necessary to overcome the problems of instrument design imposed by the use of environmental cells, and for the assessment of their value in biology.

High Resolution Microscopy

Here we consider high resolution microscopy separately on two counts: (i) different mechanisms of imaging and of contrast formation are predominant at high resolutions, and (ii) the highest resolutions are primarily of importance to the biologist in the study of macromolecules (including viruses). (For investigations at the cellular and subcellular level, of course, problems of specimen preparation and handling are the limiting factors and the highest resolutions are unnecessary.)

There are strong incentives within the physical as well as the biological sciences for the development of high resolution instruments, and advances are likely to come from the convergence of improvements in design now being sought in many programmes rather than from any radically novel departure (though the scanning transmission electron microscope permits a substantially novel approach to high resolution). Whereas at relatively low resolutions the electron image is formed primarily by amplitude contrast, which is the consequence of the scattering of electrons by the specimen, phase effects predominate at high resolutions. Phase changes introduced into the electron beam by the specimen combine with phase changes introduced into the incident beam by the objective lens of the instrument to give an amplitude contrast at the imaging plane. The attainable resolution is limited by spherical aberration effects in the objective lens. Much high resolution technology is directed towards limiting its effects, for instance by use of quadrupole and octopole lenses, or by the use of high frequency currents to energize the electron lens. Alternatively one can accept the consequences of spherical aberration, but seek to isolate them from the useful information carried in the electron beam by introducing a suitably designed and located zone plate. Calculations indicate that at 200 kV, zone plates could increase resolution at the 0.2 nm level by about 0.05 nm. A different approach makes use of the fact that all the useful information about the specimen is contained in the image, even though it is masked by spherical aberration and other effects. Knowing the characteristics of the lens system the information recorded on the photographic plate can be translated into digital form and computer techniques used to sort out the useful information. Computing equipment of high capacity is needed at relatively low levels of accuracy.

High resolution microscopy is also limited by chromatic aberration of the lens. In principle this can be minimized by suitable design of the electron lens (the use of superconducting lenses has been mooted in this connexion), but it is unavoidable in heterogeneous specimens of appreciable thickness, such as are often necessary in biological specimens if contrast is to be adequate. Several approaches are being made to improved contrast. The use of low voltages is being explored, but is open to many of the objections that are leading into work at increasingly high voltages. The use of phase plates may be more promising: a suitably designed plate can enhance contrast without significant loss of resolution. Strioscopic methods are also of potential value for high resolution work.

High resolutions demand very accurate instrumentation and are inherently costly. They demand very stable beam voltages and lens currents and high mechanical stability. Problems of preparing and handling the minute specimens which are necessary are especially acute, and the need for extremely thin support substrates may be another limiting factor.

A different approach to high resolution uses scanning electron microscopy, in which a fine beam of electrons is traversed point by point across the specimen, allowing the detail of the interaction of the electron beam with each part of the specimen to be observed separately. This contrasts with the conventional microscope in which the whole area of the specimen is exposed to the electron beam, and all points of the image are generated simultaneously on the viewing screen. Scanning instruments are already well established in which signals produced by reflected electrons, X rays, or light are used to build up an image of the surface of the specimen. Recently, however, the availability of very bright electron sources has made possible the development of scanning instruments operating at high resolution in the transmissive mode. With such instruments the number of transmitted electrons of any particular category can be isolated and counted separately for each point of the specimen. This can yield much information about the characteristics of individual points—for instance, the ratio of inelastically to elastically scattered electrons is directly accessible, and provides a means for measuring the average atomic number of the material excited by the probe. As the scanning transmission microscope involves no lens between specimen and detector, restrictions on its accuracy due to chromatic aberration do not arise, and the resolution is limited only by spherical aberration, diffraction effects, and by the size of the probe. Probe diameters of 0.5 nm have already been achieved with field emission guns.

To visualize individual biological molecules higher voltages than are now used may be necessary: the range between 100 kV and 500 kV has been suggested as a compromise between theoretical requirements and the need to avoid gross radiation damage, though still higher voltages may be practicable. The hypothetical system using a zone plate would, it has been suggested, be just capable under ideal conditions of imaging labelled bases of short strands of polynucleotides in unstained specimens, but greater hopes are held out for the study of enzyme substructure, and the visualization of active sites labelled by heavy atoms.

High Voltage Electron Microscopy

The chief incentive for working at high voltages is the greater depth of specimen preparation that they allow, which with biological materials is nearly proportional to the applied voltage. This increase in penetration makes it possible to investigate the three-dimensional ultrastructure of chromosomes in specimens 1.5 μm thick. Under favourable conditions even thicker sections have been studied.

The theoretical resolving power advantage of an electron microscope is nullified in practice by problems of electrical and (particularly) mechanical stability. Contrast falls off rapidly with increasing voltage, so that image intensification techniques may be necessary to give a useful picture of thick specimens. The large depth of focus means that a great deal of information is projected on the two-dimensional viewing screen, and special methods of image analysis may be necessary to obtain a comprehensible picture.

The most desirable operating voltage is still a matter of doubt. Several instruments have been built in the range 1 MV and above, but it has been proposed that the range up to 500 kV, within which chromatic aberration effects already show a substantial improvement, should be explored. Economic considerations are important here: a rough guide is that in the high voltage range the cost of the instrument is proportional to the operating voltage.

Image Analysis

The almost universal practice in electron microscopy is to preserve morphological information in the form of amplitude contrast in the electron beam, and to observe the image on a fluorescent screen or record it on storage cathode ray tubes, magnetic tape or photographic plates. Methods are being devised by which information is directly converted to digitalized form in which it can be processed without photographic recording, but photographic plates are at present the most efficient recording technique and are used at every level of resolution. A recurrent problem in the study of all but the thinnest specimens is that information about a three-dimensional object is recorded as an image in two dimensions. As a conventional instrument has a depth of focus of at least several hundred nm, this means that the final image is a superposition of all the features along the direction of the beam within its depth of focus, without any perspective effect. Some way must therefore be found of extracting the contribution from different levels in the specimen.

When working at comparatively low resolutions it is possible to cut several thin sections, observe them as two-dimensional objects and combine the serial images to give a three-dimensional representation of the specimen. Alternatively stereomicrographs can be produced from pairs of pictures of the same area of the specimen, inclined to each other at a suitable angle; this is especially useful in high voltage electron microscopy. Recently, direct stereoviewing has been developed for use in the scanning microscope.

To acquire more detailed information about structures more sophisticated methods are necessary. All the information extracted from the specimen by the electron beam is preserved in the electron micrograph: the problem is to extract and interpret it. The amplitude contrast information contained in the optical diffraction pattern of the electron micrograph can give information about periodicities in the object (and can, incidentally, "clean up" the image by eliminating background caused by specimen irregularities and present information not readily detectable by eye). For greater detail phase contrast information, which is in principle accessible by holographic methods, must be used; although these have been mooted for many years they are only now showing promise of being a practicable proposition. More has been achieved from a digitized array of optical densities of the image obtained by microdensitometry. By analysing a (calculable) number of planar projections it is possible to reconstruct the three-dimensional image. The number of projections needed depends on the degree of symmetry of the object, and most work has been done with objects such as negatively stained spherical viruses, where a few projections are sufficient to resolve a particle of about 20 nm diameter to 1 nm, the limit of resolution attainable with negative staining. For substances with helical symmetry such as muscle filaments sufficient information for structural analysis can be obtained without measuring or analysing phases. Although the amount of computation necessary for objects of low symmetry is great, there is no reason in principle why this method should not be applied to any structure. An acceptable micrograph contains about 10^6 picture elements and can record up to twenty grey levels (a commercial television operates with five). Rapid computational techniques have been developed which make the processing of information at this level of detail a practical proposition, and it has been proposed that the necessary computing equipment should be made integral with the electron microscope. With improved methods of specimen preparation and preservation, and with the use of faster computers of higher capacity, the three-dimensional analysis of biological structures, such as ribosomes, at still higher resolutions should be a practicable proposition.

Microanalysis

When a high energy electron beam, such as is used in conventional transmission and scanning electron microscopy, interacts with matter, characteristic X rays are produced. If the beam can be brought to a fine focus it affords a means of analysing a very small surface area, for X radiation from atoms, even of closely similar atomic number, can, in principle, be sharply resolved and accurately quantified in a spectrometer.

In practice the efficiency of X-ray microanalysis is limited by background noise in the signal (especially important in biological materials, the elements of interest are usually at low concentrations) and by the measuring efficiency of the detector. X-ray detectors are of two kinds—wavelength diffracting spectrometers and energy-selective analysers. Crystal diffractometers are capable of accurate analysis, but their collecting power is limited by basic optical considerations and by problems of design. Energy analysers have low quantum resolution, and their response to monochromatic radiation takes the form of electrical impulses distributed about a mean amplitude, which, especially with light elements of biological interest, are vulnerable to interference from background radiation. On the other hand, they are capable of much higher collecting powers than are crystal diffractometers.

With currently available detectors the minimum amount of an element in a biological tissue that is measurable by X-ray microanalytical methods is about 10^{-18} g and the minimum weight/weight ratio (in the volume exposed to the microprobe) about 100 p.p.m. This puts a lower limit on the size of specimen that can be exposed to a probe and give a useful signal. The spatial resolution of X-ray analysis is also restricted by the spread of excitation in a (thick) specimen exposed to the beam: in typical operating conditions a probe 1 µm in diameter will excite a volume of about 5 µm depth and diameter. This difficulty can to some extent be mitigated by working with specimens of thickness between 0.5 and 5 µm, when excitation will occur with a cone 1 µm or less in thickness. With very thin sections (150 nm or below) still higher resolutions can be achieved, but at the expense of now exciting a small volume and producing a small flux of X radiation.

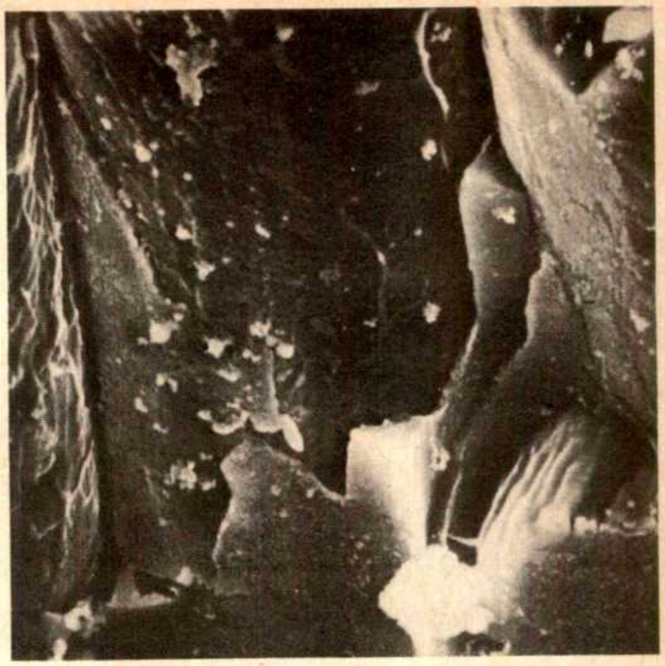

Fig. 3 Cryofractured *Vicia faba* root (×2,000) which has been treated in the same way as described in Fig. 2. The cryofractured leaf in Fig. 2 shows the correct orientation and juxtaposition of the cells and demonstrates that the watery cell contents are still present, but in the frozen state. The root picture here shows part of the wall torn off revealing the underlying cytoplasm. Part of the intercellular space, which would be filled with liquid in the living state, can also be seen.

This discussion relates to probes formed from the hot tungsten filament electron emitter which until recently was invariably used in electron beam technology. They have an inherent maximum brightness, so that a spot size of 10 nm is needed to give an image in a reasonable time. Recently brighter sources have been developed. Sources using rare-earth borides are two or three orders of magnitude brighter than tungsten filaments and the field emission gun is several orders brighter still. It should make a spot size of 2 nm diameter a feasible proposition, but the current at present attainable in so small an area is likely to prove insufficient for microanalysis except perhaps for high elemental concentrations.

An important typical biological application of microanalysis is the determination of the distribution and movement of ions and other species in cells and tissues. Currently available technology should allow ion concentrations within organelles, between different parts of the cytoplasm and across cell boundaries to be measured. Resolutions an order of magnitude better might lead to better measurements of concentration gradients across individual membranes and even within the membrane itself. This could provide important evidence to moderate between current rival theories of the mechanism of membrane action.

As in other biological applications of electron beam technology, problems of specimen preparation predominate in microanalytical investigations of this kind. The basic problem is to ensure that the intracellular ions being studied stay where they were in the living cell throughout the preparative procedures. It seems at present that the only promising technique involves the use of frozen sections, with the inherent difficulties of preparation and handling.

Progress in the application of electron microscopy to biological problems depends both on advances in instrument technology and on knowledge of how to apply those advances to the study of biological systems. At present the latter lags behind, and much of the potential of electron beam technology is frustrated because the biologist cannot yet use it. Work is especially urgently needed in studies of the radiation damage of biological materials and of methods of specimen preparation and manipulation. This will involve the interaction of a wide range of scientific disciplines.

The principal directions of development of biological electron microscopy are towards structural studies at higher resolutions and the development of accurate analytical techniques. The immediate biological applications of the former fall primarily in the field of molecular biology. Analytical techniques are likely to prove very important in studies at the cellular and subcellular level.

Much also remains to be done in the use of established instruments in biological work, and improvements in their performance and design, and the development of ancillary equipment, will all extend significantly the scope of the types of instrument already established.

Figure 1 was taken by Dr Nigel Unwin at the MRC Laboratory of Molecular Biology, Cambridge. This paper is a shortened version of a report commissioned by the Biological Sciences Committee of the Science Research Council.

Legacy of van der Waals

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It is a hundred years since van der Waals related the pressure, volume and temperature of a fluid by the equation which bears his name. This article, which is based on a lecture delivered at an Institute of Physics Conference at the University of Kent in April, describes the background and present value of his work.

JOHANNES DIDERIK VAN DER WAALS never learned Latin and so was barred from the regular university course in his home town of Leiden. He studied part time, but it was only after new legislation that he was able to present a thesis in June 1873, at the age of thirty-five. Three years later he was offered the chair of physics in the new University of Amsterdam, where he lived until his death in 1923.

His thesis[1–5] and more than a hundred papers which followed it dominated the study of liquids until 1914. There was then a rapid loss of interest until he was remembered only for the equation of state which had been the climax of his thesis. The purpose of this article is, first, to put what he wrote in the context of its day and, second, to examine the ideas which have flowed from his work and to show why there has been recently such a revival of interest in it.

His Predecessors

By 1873 physicists had substantially correct ideas of molecular speeds, masses and sizes[6,7]. Clausius, Maxwell and Boltzmann had tackled, with some success, both the equilibrium and transport properties of the dilute gas, but even the equilibrium theory of denser fluids was still in a primitive state. It was known that gases other than hydrogen were more compressible than Boyle's law required, that this compressibility was due to intermolecular forces stronger but of shorter range than gravitation, and that it was the space occupied by the molecules which made hydrogen a "fluide élastique plus que parfait"[8]. In the eighteenth century[9] Bernoulli had proposed that in Boyle's law the specific volume v be replaced by $(v-b)$, where b was thought to be the volume of the molecules. Hirn[10,11] (1863), Dupré[12] (1869) and others revived this proposal, but van der Waals tackled the problem anew by calculating the effect of molecular size on the mean free path. He thus showed that the covolume b (the name is due to Dupré (ref. 12, page 61; see also ref. 13)) is four times the volume of the molecules, although he realized that the substitution of $(v-b)$ is valid only at low densities, that is, at the level of the second virial coefficient in modern language. (Rayleigh[14,15] was apparently the first to see that the substitution of $(v-b)$, when b is the volume of the molecules, is exact in one dimension at all densities.) Later he tried to calculate the covolume for denser fluids but his results had to be corrected by Boltzmann and van Laar[16]. This problem is still unsolved, and could not even be tackled systematically until the development of graphical expansions between 1920 and 1940.

His calculation of the effect of the attractive forces on the pressure was more fruitful. Young and Laplace had known that these were responsible for the surface tension of a liquid. The latter showed that the pressure in a drop of radius l could be written $(K+H/l)$, where K and H are integrals, over the separation r, of the mutual force between two elements of liquid. He put the density equal to "unity", but those who followed took the force to be proportional to the mass in each volume element, and so multiplied his results by the square of the density. Laplace's modified results, obtained both by Dupré, helped by his colleague F. J. D. Massieu (ref. 12, pages 147, 150–157), and by van der Waals, can be written in modern notation by supposing there to be a potential $u(r) \leqslant 0$ between each pair of N molecules in a volume V

$$K=-\tfrac{1}{2}(N/V)^2\int u(r)\mathbf{dr} \qquad H=-\tfrac{1}{4}(N/V)^2\int ru(r)\mathbf{dr} \tag{1}$$

(Before about 1880 there was a casual attitude to units and dimensions which can make it difficult to decide what was meant. This difficulty probably led to Rayleigh's mistaken assertion[17] that Dupré found K to be proportional to density. van der Waals sometimes omits the factor of the square of the density.)

Young estimated K at several thousand atmospheres, a result which Dupré confirmed by showing that it is $(\partial U/\partial V)_T$ in a liquid, where U is the *travail de désagrégation totale*, or configurational energy. Since U is zero at zero density

$$U=-KV=\tfrac{1}{2}(N^2/V)\int u(r)\mathbf{dr} \tag{2}$$

and so, by purely thermodynamic argument

$$Tf(V)=p+K \text{ or } p+a/v^2 \tag{3}$$

Dupré obtained equation (2) for a liquid in his book, but not equation (3). He died in 1869, the year it was published Others had, without such thorough discussion, also proposed an internal pressure proportional to the square of the density[18–21]

In 1863 Hirn[10,11] had written

$$(p+\Phi)(v-b)=RT \qquad (4)$$

but although he realized that Φ greatly exceeded p in a liquid, and that it might be a function of volume only, he never wrote it as a/v^2

van der Waals's Equation

van der Waals proposed

$$(p+a/v^2)(v-b)=RT \qquad (5)$$

He did not use his derivation of Laplace's K to obtain directly the term a/v^2, but justified the latter by a simple argument repeated today in most textbooks Only towards the end of the thesis did he tentatively identify a/v^2 with K, at least for carbon dioxide, but he followed this by other less useful relations between K and the equation of state, which he omitted when the thesis was translated (ref 1, pages 97–99)

At first sight he seems to have done no more than to combine some current ideas Why then did his work have so great an influence? First, because his ideas were clearer than those of his predecessors He understood, as they did not, the new kinetic theory of gases, and so was able to obtain the correct covolume He used Clausius's virial theorem[22] of 1870, together with Laplace's static view of matter, in a way which appealed to his contemporaries even if it did not always convince them

Second, his work came soon after the discovery of the continuity of the gas and liquid states by Andrews[23,24] Hirn and Dupré had tried to represent only the pressure of gases, they discussed liquids also but could not, before 1869, have aspired to fit both states with one equation This van der Waals did, and the influence of Andrews is unmistakable—his title is a translation of that of the Bakerian lecture[23]

His equation is a cubic in v and so has either one or three roots for a given p and T There is one if the temperature exceeds the critical, that is, if $RT > RT^c = 8a/27b$ There are three at lower temperatures, the smallest and largest of which are liquid and gas, but not necessarily in their saturated states Thus the equation represents both Andrews's continuity of state and the sigmoid loops which his colleague James Thomson had already proposed as a continuous isotherm in the two-phase region[25]

Although written in Dutch, the thesis received immediate attention in Britain Andrews called on one of his daughters to help, and in February 1874 wrote to Thomson[26] from Belfast that "Bessy and I are hard at work on Diderik van der Waals!" Maxwell first noticed it publicly in June 1874 in a review[27,28] of a book by Plateau, whose macroscopic approach he contrasted with the molecular picture of van der Waals In October he reviewed the thesis[29,30] favourably, and next year showed how the saturated volumes and the vapour pressure p_σ could be obtained from the sigmoid isotherms[31–33] His construction was the "equal-area" rule, the line $p=p_\sigma$ is drawn to cut the sigmoid curve so that the area of the loop above p_σ is equal to the area of that below

The link between Leiden and Belfast was strengthened when van der Waals's professor, P L Rijke, sent W J Janssen to learn from Andrews the techniques of studying fluids at high pressures Janssen took equipment back to Leiden where he repeated for nitrous oxide Andrews's work on carbon dioxide This he presented to the British Association meeting in 1876, when Andrews was President[34] From this modest beginning grew the great Dutch schools of experimental work on the equation of state at Leiden and Amsterdam

Recognition came more slowly in Germany As late as 1876 Clausius[35] made a further calculation of the covolume and, not knowing of van der Waals's result, made it eight times the volume of the molecules van der Waals quickly corrected him[36] (In his review[29,30] Maxwell had criticized van der Waals's result and gave, without derivation, an expression which is equivalent to sixteen times the volume!) In 1877 Wiedemann published a long abstract of the thesis in German[37], which was soon followed by Roth's translation[2] of the whole

Once the value of the new equation became clear it was examined more carefully, with particular attention to the separation van der Waals had made between the two effects of molecules occupying space and of attracting each other, a separation which is at the root of what are now called mean-field and perturbation theories

Mean-field Theories

When is the separation justified, and the calculation of U from equation (2) valid? The answer is for hard spheres with an attractive potential of so long a range that each interacts with many others U can then be found correctly by averaging $u(r)$ over all configurations without regard to the microscopic structure of a dense fluid Today this structure is described by a probability density $g(r)$, the ratio of the local density at distance r from a given molecule to the mean density Hence

$$U=\tfrac{1}{2}(N^2/V)\int_0^\infty u(r)g(r)4\pi r^2\mathrm{d}r \qquad (2')$$

and equation (2) follows if $g(r)=0$ for $r<\sigma$, the diameter of a sphere, and $g(r)=1$ for $r>\sigma$

van der Waals knew that his results depended on such an assumption, for he wrote (ref 3, pages 343, 361 and 435) "On the particles of a gas no forces act, on the particles within a liquid the forces neutralize each other", and again, that in a liquid "the energy will be the same for all positions which it [the particle] is free to assume" In modern terms, if $g(r)=1$, the potential of average force is zero Neither he[3] nor Maxwell[38] was so clear that putting $g(r)=1$ is justified only if $u(r)$ is weak but of long range Rayleigh[14,15] was more precise, there must be forces "whose range, though small in comparison with the dimensions of sensible bodies, is large in comparison with molecular distances In the extreme case, the influence of the discontinuous distribution of the attractive centres disappears, and the problem may be treated by the methods of Laplace" Boltzmann was equally clear, in the first chapter of the second volume of his *Vorlesungen über Gastheorie*[39] he says the forces must be weak but of long range When van der Waals saw this in proof he objected that he had never made this assumption, and that he doubted if it were true Indeed, in his thesis[3], he had used the fact that $2H$ is the first moment of K to show that the effective range of $u(r)$ is only 3 to 6 Å Boltzmann replied[39] that "Nevertheless, I cannot obtain an exact foundation for his equation without this assumption" He was followed by Ornstein in 1908 (see refs 40 and 41, both of which refer to his thesis) in the first derivation of van der Waals's equation from Gibbs's statistical mechanics The modern version of this work is that of Kac and others[42–45] who have shown rigorously that the "van der Waals limit", as they call an equation of the form of equation (3), is implied by a potential

$$u(r)=-\alpha\gamma^s\exp(-\gamma r) \qquad (6)$$

where s = dimensionality, in the limit when the range γ^{-1} becomes infinite

When interactions are short, $g(r)=1$ is a drastic mean-field approximation widely used to discuss critical points, Curie points and order–disorder transitions of all kinds Domb[46,47] has pointed out that in 1889 Hopkinson discussed "the temperature at which the magnetism disappears which we may but many who then took it up seemed unaware of the past, appropriately call the critical temperature" The name Curie point was introduced by Weiss and Onnes in 1910 after the former[48–50] had, in 1906, proposed a mean-field treatment based on the reasoning of van der Waals, "On pourrait donner à NI le nom de champ intérieur pour marquer l'analogie avec la pression intérieure de van der Waals"

Mean-field approximations are surprisingly accurate except at critical points where they fail to describe the singularities of most physical properties as functions of T and v (or other extensive variable) The free energy from equation (5) is everywhere an analytic function and the behaviour it implies is most simply explored by expanding it in a Taylor series in $(T-T^c)$ and $(v-v^c)$ This was done by van der Waals[51,52] in 1894 and in more detail by Verschaffelt[53–54] in 1902 The failure of this simple Taylor expansion to describe the critical point was clear by the beginning of this century and in 1923 Verschaffelt[55] devised an expression for the pressure which had some of the required singularities, but interest was now waning and his work was not followed up When critical phenomena again became an active field after 1950, one of the first attempts[56] to devise an acceptable form of the pressure was similar to that of Verschaffelt Later work[57] has led to more satisfactory functions, the so-called scaling functions, the description of which is outside the scope of this article

Perturbation Theories

If $u(r)$ is everywhere weak then $y=|u(r)/kT|$ is small and so a perturbation expansion in y is a natural way to calculate the phase integral In the van der Waals limit y tends to zero and only the first term contributes to the thermodynamic properties If, however, $u(r)$ is, more realistically, of a range comparable with σ and has a minimum of $-\varepsilon$ then $y_{\max}=\varepsilon/kT$ is of the order of unity at the critical point It is now not obvious that an expansion will converge rapidly, but fortunately it does so If the initial potential is that of a hard sphere, this can be "perturbed" into a realistic form by adding an attractive term[58] and softening the repulsion[59] Barker and Henderson and others[60,61] have used such perturbation expansions to obtain a quantitatively successful theory of fluids. Their success depends on the fact that $g(r)$ in a dense fluid is determined chiefly by the geometry of packing of the hard cores, and so, to the first approximation, U can be found from equation (2′) by putting $g(r)$ equal to $g_0(r)$, the distribution function for the hard spheres This step is in direct descent from van der Waals's separation of the attractive and repulsive forces[62]

Principle of Corresponding States

Substances to which equation (5) applies conform to a principle of corresponding states, for the three critical constants can be expressed in terms of R, a, and b van der Waals[63] established this in 1880 and the principle at once became a useful tool in deciding how to liquefy the so-called permanent gases, for it enabled critical and Joule-Thomson inversion temperatures to be estimated[64] He always associated the principle with the two parameters a and b of his equation, but today we accept it as the consequence of a set of conformal intermolecular potentials, that is, those of a common geometric form with two scaling parameters σ and ε Kamerlingh Onnes and others[65–67] suggested that a condition of mechanical similarity lay behind the principle, but a clear statement[68,69] of this condition came only in 1938

Surface Tension

If the first Laplace constant K leads, by way of equation (2), to van der Waals's equation, what can be found from his second constant H? Laplace supposed that a liquid has a sharp surface at which the density falls abruptly from that of the liquid to the negligible density of the gas This assumption was made later by Fowler[70] who thereby obtained

$$\gamma=1/32\,(N/V)^2\int r^2(\mathrm{d}u(r)/\mathrm{d}r)g(r)\mathrm{d}r \qquad (7)$$

If again we put $g(r)=1$ and integrate by parts then we obtain, with Laplace and van der Waals, $\gamma=\frac{1}{2}\mathrm{H}$

Laplace's derivation was criticized by Poisson for the assumption of a sharp interface, and Fowler's similarly by Kirkwood and Buff[71] who obtained a more generally valid form of equation (7) in which $g(r_{ij})$ is a function of the positions in the interface of molecules i and j

van der Waals came also to realize that this change of density with height must be taken into account, but his method of doing so was different[51,52] He assumed that the free energy contained terms proportional to the derivatives of the density ρ with height z and so, by arguments too long for summary, found

$$\gamma=-C\int\rho(\mathrm{d}^2\rho/\mathrm{d}z^2)\mathrm{d}z=C\int(\mathrm{d}\rho/\mathrm{d}z)^2\mathrm{d}z \qquad (8)$$

The parameter C is proportional to the second moment of $u(r)$, not the first moment H, as for a surface of zero thickness Maxwell had attempted to obtain expressions of this kind, but his work was criticized by Rayleigh[72] who arrived independently at essentially the same result as van der Waals

This approach was revived by Cahn and Hilliard[73] and, in the hands of Widom and others (refs 74–76 and work by J Yvon cited there), is now the principal tool for studying surface tension in the critical region where the thickness of the interface becomes long compared with the range of $u(r)$ The parameter C, the second moment of $u(r)$, becomes the second moment of the direct correlation function $c(r)$ in the modern version[74–77] That the range of $u(r)$ and $c(r)$ is the same is the Percus-Yevick approximation

Theory of Mixtures

From 1889 to 1912 van der Waals worked on the extension of his equation to mixtures[5,78,79] In principle this is simple, because a and b arise from binary interactions they become in a mixture of composition x

$$a_x=\sum_i\sum_j x_i x_j a_{ij} \qquad b_x=\sum_i\sum_j x_i x_j b_{ij} \qquad (9)$$

He thus found an equation which, by choice of the parameters a_{ij} and b_{ij}, could, even for a binary mixture, represent a great number of phase equilibria in systems with up to three fluid phases and three critical lines[80] His theory led to a big experimental programme at Leiden and elsewhere in which these complications were unravelled[79,81] After 1914, however, physicists forgot both theory and experiments, which had to be rediscovered by chemists and chemical engineers after 1945 In 1962 Leland recovered equation (9), in its modern guise with the inter-molecular parameters $(\varepsilon_{ij}\,\sigma_{ij}^3)$ for a_{ij} and (σ_{ij}^3) for b_{ij}, but it was a further six years before it was reidentified as the van der Waals approximation[82,83] This equation, together with closely related perturbation expansions[84–87], are now the most satisfactory theory of fluid mixtures

Legacy

In each of these fields the ideas of van der Waals and his school lie behind much of modern work, and it is worth asking why they were so neglected after 1914 First, perhaps, because there were then new fields to explore The Dutch experimental school turned to low temperature physics, and theoreticians everywhere to quantum mechanics Second, there was an impasse in the theory of fluids because of ignorance of the origin and form of $u(r)$, a difficulty which needed quantum mechanics for its solution By 1930 the field was open again, and often explored what turned out to be the blind alley of lattice theories With hindsight, however, the reintroduction of the ideas of the van der Waals era can be plotted in more precise form No exact priorities can be given but, in outline, the timetable runs as follows Taylor expansions about critical points (1935, 1937 (refs 88 and 89)), the theory of the pair distribution function (1935 (ref 90)), of surface tension (1937 (ref 70)), 1948 (refs 74–76), 1949 (ref 71), 1958 (ref 73), of conformal potentials and corresponding states (1938–1939 (refs 68 and 69)), non-lattice theories of mixtures (1951 (ref 84)), 1962 (ref 82), 1968 (ref 83), the direct correlation function (1953 (ref 91)), and perturbation theories of pure fluids (1954 (ref 58)), 1963 (refs 42–45), 1964 (ref 59), 1967 (refs 60 and 61) Other ideas, not discussed here, have played at least as important a part in the current renaissance of liquid state physics, but in the papers cited above one can see the true legacy of van der Waals and his school

I thank Dr H J Michels, Miss V A Milne and Professor J G Powles for their help

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Cover Cartoon

The cover illustration of this issue of *Nature* depicts the British Association for the Advancement of Science as seen through the eyes of a *Punch* cartoonist in September 1865 when the association held its annual meeting in Birmingham At that time, Sir Roderick I Murchison, who is seen conjuring in the foreground of the cartoon, was President of the Geology Section Presumably Professor T H Huxley and Dr Richard Owen are the two gentlemen embracing each other

Identification this far is easy, but the names of the remaining scientists pose problems Who indeed are the geologists demonstrating, before their time, the subtleties of plate tectonics? And who is that brandishing what looks suspiciously like a red hot poker? The caption to the cartoon poses a problem as well "The British Association illustrated by experimental conjuring (a box of tricks packed up in a large clothes-basket for doing the Stodare trick Swords separate)" Who or what was Stodare? The first reader to convince the Editor—by letter—that he can identify the scientists and also interpret the caption will receive a free subscription to *Nature* for a year

Prebiotic Activation Processes

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A series of reactions involving urea, imidazole, and magnesium can result in the activation of nucleotides and amino acids to form polymers. Unlike any which have been suggested before, these reactions have parallels in contemporary biological mechanisms.

PREBIOTIC syntheses of many of the twenty naturally occurring amino acids and of the four standard ribonucleotides have been described[1,2]. It seems natural, then, that we next ask how these compounds were induced to combine to form polypeptides and polynucleotides. Here we suggest a possible solution to a simplified but well defined version of this problem, the activation of a simple mixture of amino acids and nucleotides. The prebiotic soup, no doubt, contained many other compounds, some of which would have complicated the reaction scheme that we propose. We think, however, that a discussion of this oversimplified problem is a necessary introduction to any treatment of a more realistic prebiotic soup.

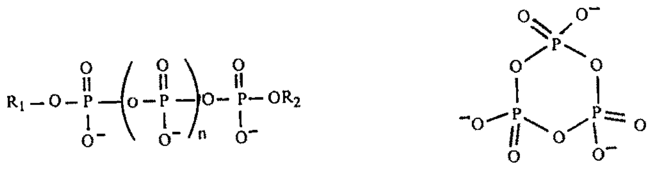
Two groups of prebiotic condensation reactions have previously been discussed extensively. In the first, monomers are heated together in the absence of water[1,3]. In the second, unsaturated molecules such as cyanamide[1,4] and cyanoacetylene[5] are used as dehydrating agents in aqueous solution. Neither of these groups of reactions resembles contemporary biochemical pathways.

Here we describe a series of reactions that have much in common with the activation steps that precede protein and nucleic acid synthesis. Each reaction occurs in the solid state in plausible prebiotic conditions. Together they provide the basis for a unified scheme of amino acid and nucleotide activation. Urea, imidazole and Mg^{2+} are at present essential catalytic components of our reaction mixtures, but it is probable that other organic molecules could replace them.

Chemical Nature of the Primary Energy Reserve

The energy for most biological syntheses is provided by the hydrolysis of pyrophosphate bonds. ATP is the main energy source, but other compounds, for example GTP, are used occasionally. It seems unlikely that a highly specific synthesis of ATP or GTP occurred on the primitive Earth. Instead, we propose that the primary chemical reserve of free energy on the primitive Earth was a mixture of inorganic and organic polyphosphates.

This proposal is not new[1,2], but it is made more plausible by the discovery of a reaction in which urea, in the presence of NH_4^+, catalyses the formation of inorganic and organic polyphosphates from inorganic phosphate at temperatures as low as 65° C[6-8]. The arguments that follow, however, do not depend on the way in which the polyphosphates, that we assume to have been present on the primitive Earth, were formed. They could have been made directly from an acidic phosphate in a volcano, or by some undiscovered catalytic or photochemical process, rather than by the urea-catalysed condensation. To make the discussion more concrete we shall nonetheless suppose that the polyphosphates available on the primitive Earth were of the types formed by heating mixtures containing urea, ammonium phosphate and metal ions in various proportions at moderate temperatures[8] (Fig. 1).



I II

Fig. 1 I, $R_1=R_2=H$, $n=0, 1, 2$ inorganic phosphate R_1=Nucleoside, $R_2=H$, $n=0, 1$ nucleoside di- and triphosphates R_1=Nucleoside, R_2=nucleoside, $n=0$ dinucleoside pyrophosphate II, Inorganic trimetaphosphate

Inorganic Catalysts

Pyrophosphates do not react readily with amino or carboxyl groups in aqueous solution. Thus it is hardly surprising that the coupling of the hydrolysis of linear polyphosphates and the formation of peptide bonds in aqueous solution is inefficient. Furthermore, we have found that very little reaction other than breakdown occurs if a dry mixture of glycine and the sodium salt of ATP is warmed.

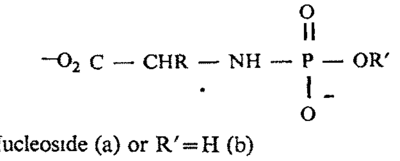
Lowenstein has reported that acetate ion can be phosphorylated by ATP in aqueous solution, in the presence of divalent ions, to give acetyl phosphate[9]. The dismutation of ATP to ADP and higher polyphosphates in the presence of catalysts has also been reported[10]. This led us to examine the behaviour of amines including amino acids, when warmed gently with the magnesium salt of ATP in solution and in the solid state. In this way one of us (R. L.) discovered a novel and general series of solid-state reactions.

Amines, including ammonia, glycine and ethylenediamine, react with ATP or AppA in the dry state, if enough Mg^{2+} is present, to form phosphoramidates

$$RNH_2+ATP\rightleftarrows RNHpA+P_2$$
$$RNH_2+AppA\rightleftarrows RNHpA+pA$$

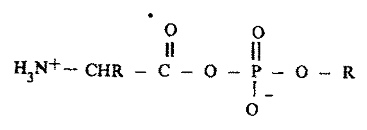
Imidazole reacts in a precisely parallel fashion to form ImpA. The yields in these reactions range from a few % in the case of imidazole to 40% in the case of ethylenediamine. We do not yet know how general this catalytic action of Mg^{2+} is, nor have we studied the phosphoramidates of the type $RNHPO_3H^-$ that are presumably formed along with the adenylic acid derivatives. Our results show, however, that, if the prebiotic soup were rich in Mg^{2+}, polyphosphates would have reacted with amino acids on evaporation to form derivatives of the type shown in Fig. 2.

III



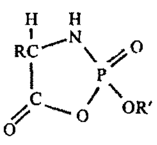
$$^{-}O_2C-CHR-NH-\underset{O^-}{\overset{\overset{O}{\|}}{P}}-OR'$$

Fig. 2 R'=Nucleoside (a) or R'=H (b)



$H_3N^+-CHR-\overset{\overset{O}{\|}}{C}-O-\underset{\underset{O^-}{|}}{\overset{\overset{O}{\|}}{P}}-O-R$

IV



V

Fig. 3

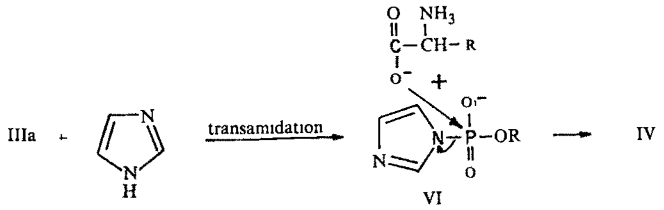


Fig. 4

There is another plausible prebiotic source of phosphoramidates of the special class IIIb, namely, the reaction between amino acids and inorganic trimetaphosphate in aqueous solution[11] or in the solid state (N M Chung, unpublished) This reaction, however, cannot be extended to the production of amidates or nucleotides

Organic Catalysts

The phosphoramidates discussed in the previous section are activated at the phosphate group The phenylalanine adduct of d-pApA has been reported to condense to short oligonucleotides on a poly (U) template[12] In our studies of template-directed synthesis we have found the imidazole derivative of pA condenses very efficiently on a poly (U) template to give di- and short oligonucleotides[13]. Thus the Mg^{2+}-catalysed reactions of amino acids (or any other amine or imidazole) would provide nucleotide derivatives that can take part directly in prebiotic polynucleotide synthesis

The problem of amino acid activation, however, remains to be resolved Although the phosphoramidates of the amino acids are energy-rich compounds, they cannot react directly to form peptides, as the carboxyl groups are not activated The following considerations, however, suggest that, in the presence of an appropriate catalyst, the N-phosphorylated amino acids might behave kinetically as though they were carboxyl-activated

Phosphoramidates are exceedingly resistant to hydrolysis in alkaline solution, while the aminoacyl adenylates IV (R= adenosine) (Fig 3) are extremely labile, the rates of direct hydrolysis probably differ by a factor of 10^5 or more at room temperature and *p*H 8 5 On the other hand, the free energy content of the anhydride is not likely to exceed that of the phosphoramidate by more than 5 kcalorie This suggests that at least 1/10% of the anhydride would be in equilibrium with the phosphoramidates at room temperature Thus, if equilibrium were approached rapidly enough, a phosphoramidate of an amino acid would behave kinetically as an aminoacyladenylate This is an interesting possibility because aminoacyladenylates are the intermediates in protein synthesis

The phosphoramidate III could be converted to the anhydride IV by an intramolecular or by an intermolecular mechanism Ring compounds such as V (Fig. 3) would be involved in the intramolecular route, they have been discussed a number of times in related contexts[14] Here we consider the alternative intermolecular mechanism (Fig 4), because it provides a simple explanation of some of our recent results

If the phosphoramidate III (R=H, CH$_3$) is heated (65–100° C) alone no peptide is formed, but in the presence of excess imidazole di- and short oligopeptides are formed in yields of up to 10% A possible mechanism involves the formation of ImpA (VI) as an intermediate (Fig 4)

We have confirmed that a higher yield of peptide is obtained when ImpA is heated with glycine in the same conditions, and that carboxylic acids like benzoic acid react with ImpA to give the anhydride of benzoic and adenylic acid It is also interesting that the synthesis of the phosphoramidate IIIa (R=adenosine) and its subsequent condensation to short peptides can be achieved in a single operation if ATP, glycine, imidazole and Mg^{2+} are heated together

If aminoacyladenylates (IV) (R=adenosine) are generated in this system they would react with free imidazole to form a certain amount of the corresponding aminoacylimidazolides VII (Fig 5) Some of the peptide formed may be derived from this reactive intermediate rather than from the aminoacyladenylate

Parallels with Biochemistry

The direct synthesis of peptides in the solid state has little in common with contemporary biochemical processes But the intermediates which we believed to be formed in the solid state do resemble contemporary reactive intermediates The aminoacyladenylates are the substrates of protein synthesis Many phosphate kinases and related enzymes form intermediates in which histidine or lysine is attached to phosphate by an N–P bond[15,16]

We propose, therefore, that activated intermediates for prebiotic condensation reactions were formed in the solid state and subsequently reacted in the presence of small amounts of water to form oligonucleotides and oligopeptides The solution reactions may have evolved into polynucleotide and polypeptide synthesis

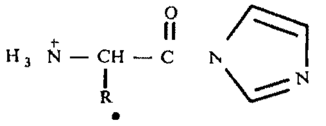
The aminoacylimidazoles and the aminoacyladenylates both react specifically with hydroxyl groups in preference to water (R Saffhill and C K Biebricher, unpublished) It is thus likely that a proportion of the activated intermediates, instead of reacting directly to form peptides, would react with adenylic acid in aqueous solution to form the 2′(3′)-ester This reaction resembles the step in protein synthesis in which the amino acid is transferred from an aminoacyladenylate to the terminus of tRNA

Our complete scheme for amino acid and nucleotide activation is summarized in Fig 6 For simplicity and to emphasize the relation to biochemistry we have written all polyphosphates as derivatives of adenosine This is not an essential part of our proposal

Prebiotic Organic Catalysts

The scheme that we propose involves imidazole as a catalyst It seems almost certain that many substituted imidazoles would behave in a similar way Potentially prebiotic syntheses of such compounds are already well known (*a*) Sugars react with ammonia in a variety of conditions to give imidazoles, particularly hydroxymethylimidazoles[17] (*b*) The adduct of ammonia and cyanoacetylene is converted to imidazole by ultraviolet radiation[18] (*c*) Sugars react with formamidine to give imidazoles Imidazole glycerol phosphate, for example, is obtained from ribose 5′-phosphate and formamidine[19] Imidazole glycerol phosphate is an intermediate in the biosynthesis of histidine[20]

Histidine is an imidazole derivative that plays a special



VII

Fig. 5

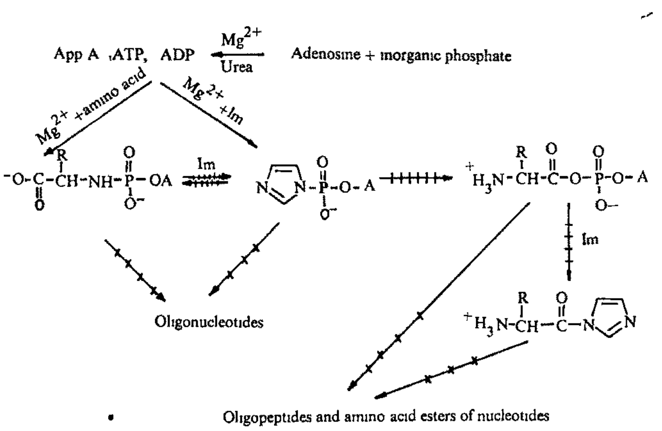

App A ,ATP, ADP
Mg2+
Urea
Adenosine + inorganic phosphate
Mg2+ +amino acid
Mg2+ +Im
Im
Oligonucleotides
Oligopeptides and amino acid esters of nucleotides

Fig 6 A scheme for the prebiotic activation of nucleotides and amino acids —→, Solid state reaction, -++→, reaction which occurs either in the solid state or in solution, -××→, reaction which occurs in solution and imitates a step in a non-biochemical sequence

role in contemporary biochemistry, as an amino acid present at the active site of a variety of enzymes. Unfortunately, no convincing prebiotic synthesis of this amino acid has been reported. If such a synthesis could be found, a detailed investigation of the catalytic properties of histidine and its peptides in this system would be justified.

No doubt, other organic catalysts exist that could replace the imidazoles, pyridines, for example. If we restrict our discussion to molecules related to those that are important in biochemistry, however, few possibilities are left for consideration. Of these, the thiols are the most interesting. Many enzymatic acylation reactions proceed through thioacyl intermediates, and thiophosphates are sufficiently activated to take part in polynucleotide synthesis. Unfortunately, very little is known about the relevant chemistry, so evaluation of this alternative must await further work on the unit reactions involved.

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Effect of Actinomycin D on DNA Synthesis in Liver

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Studies with actinomycin D do not support an essential role for transcription concomitant with nuclear DNA replication in the liver.

THE inability of purified DNA polymerases to initiate the replication of intact double stranded DNA or single stranded circles of DNA has suggested that 3′-termini must be generated as part of the initiating event. A body of evidence is now accumulating that RNA, covalently linked to DNA, provides the 3′-terminus in a variety of systems including bacteria[1-3], phages[4-7], extrachromosomal bacterial bodies[8,9], and eukaryotes[10-13]. The replication of φX174 may be an exception as its DNA formation can be initiated in the absence of RNA precursors[7] and is not blocked by rifampicin[14]. To assess the role of RNA synthesis during the S period of liver nuclei *in vivo*, the effect of a high level of actinomycin D on DNA formation has been studied in regenerating rat liver after partial hepatectomy.

Female Sprague-Dawley-derived rats were freely given food and water at all times and partially hepatectomized when they weighed about 100 g. Partial hepatectomy was the removal of 70% of the liver and, unless otherwise indicated, injections were made in the tail vein.

DNA and RNA Synthesis

To study the effect of actinomycin on ongoing DNA replication, partially hepatectomized rats were prelabelled with ^{14}C-thymidine and were then given 0.5 mg of the antibiotic. At various intervals thereafter, DNA synthesis was measured with ^{3}H-thymidine (Fig 1). The results, expressed as the ratios of the counts incorporated after and before treatment with the antibiotic, show that actinomycin caused a slow decline

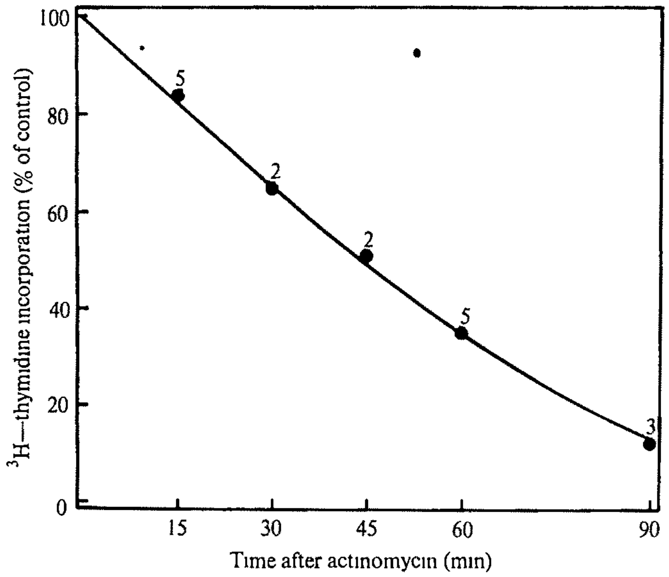

Fig. 1 Effect of actinomycin D on liver DNA synthesis *in vivo*. Partially hepatectomized rats were each given 0.1 μCi of ^{14}C-thymidine at 22 h after the operation. After 45 min, some of the animals received 1 ml of 0.15 M NaCl, the remainder 1 ml of a solution of actinomycin D (0.5 mg ml^{-1}). At 15 to 60 min after the second injection, each rat was given 5 μCi of ^{3}H-thymidine and liver samples were taken 15 min later. The values shown were calculated from the ratios of ^{3}H-DNA/^{14}C-DNA and are the averages of the individual results with two to five animals, as indicated. The average ratio for six control animals that had been given saline solution instead of actinomycin (6.2±0.4) was taken to be 100%.

in ^{3}H-thymidine uptake and that even after 45 min the reduction was only 50%.

RNA synthesis in the regenerating liver was almost completely abolished by 0.5 mg of actinomycin. Thus, the specific activities of acid-washed nuclei from rats labelled with ^{3}H-orotate (50 μCi) for 5 min beginning at 15 min after the injection of a saline solution of actinomycin were 144,000 and 1,680 c.p.m. per g of wet liver, respectively. All the radioactivity was made acid-soluble by RNase and by NaOH. Almost identical results were obtained when the ^{3}H-orotate was given with actinomycin in a single solution, indicating that RNA synthesis was stopped immediately.

The inhibition of RNA labelling by actinomycin was not due to a block in the conversion of orotate to UTP. The specific activities of regenerating liver UTP[15] at 5 min after the injection of ^{3}H-orotate (10 μCi) were 1.9×10^5 and 1.7×10^5 c.p.m. μmol^{-1} in control animals and in animals that had been given 0.5 mg of actinomycin 15 min earlier, respectively.

Autoradiographic Analysis

Partially hepatectomized rats, prelabelled with an amount of ^{14}C-thymidine (0.05 μCi) that would not interfere with autoradiography, were given actinomycin and, after various intervals, 100 μCi of ^{3}H-thymidine (Table 1). As can be seen from the ratios of ^{14}C-thymidine uptake/% of ^{3}H-labelled nuclei, most of all replicating nuclei continued to make DNA even after 60 min of exposure to the antibiotic. The ability of the replicating nuclei to incorporate ^{3}H-thymidine was lowered by the antibiotic so that the average number of grains per labelled nucleus was gradually reduced. The autoradiographic results are not consistent with the possibility that the thymidine incorporated by the rats treated with actinomycin was for the repair of DNA rather than for replication.

Rates of Elongation of DNA

The reduced uptake of thymidine in the rats treated with actinomycin was caused by a decrease in the rate of growth of DNA strands (Table 2). Thus, the incorporation of ^{3}H-thymidine into DNA and the average rate of chain elongation *in vivo* were both depressed by 90% at 1.5 h after injection of the antibiotic.

Table 2 Effect of Actinomycin on Rate of Elongation of DNA *in vivo*

Actinomycin	DNA formed (% of control)	Rate of chain elongation (nucleotide min^{-1})
−	100	1,270 (1,130, 1,410)
+	13	127 (88, 114, 178)

Partially hepatectomized rats, prelabelled with ^{14}C-thymidine (0.1 μCi), were given saline solution or 0.5 mg of actinomycin at 20 h after the operation. After 90 min, 200 μCi of ^{3}H-thymidine was injected into the mesenteric vein, liver samples were removed 1 min later, and nuclear DNA was isolated. "DNA formed" was estimated from the ratios of ^{3}H/^{14}C counts. The DNA was hydrolysed in such a way that internal molecules were released as deoxynucleotides, molecules at the 3′-OH ends of strands, as deoxynucleosides[16], and average rates of chain elongation were calculated from the ratios of thymidine/TMP that were separated chromatographically on 'Dowex' 1 (ref. 17).

With regenerating liver nuclei that are isolated and assayed under the conditions described[17,18], only nuclei that were replicating DNA *in vivo* were able to incorporate ^{3}H-TPP *in vitro*; initiation of DNA synthesis does not occur, and most or all of the DNA strands that were already growing *in vivo* elongate. The properties of nuclei isolated from animals treated with actinomycin were indistinguishable from those of control nuclei with regard to ^{3}H-TTP incorporation, deoxynucleotide and ATP requirements for DNA synthesis, and the average rate of growth of DNA chains (Table 3). To support the validity of the rate measurements *in vitro*, Table 3 shows the results obtained when actinomycin D was added to the isolated nuclei. The antibiotic caused identical inhibition of ^{3}H-TTP incorporation and of the rate of strand elongation. The results *in vivo* as well as with the isolated nuclei strongly suggest that actinomycin did not reduce the number of DNA strands that were already growing before treatment.

Table 1 Effect of Actinomycin D on Labelling of Individual Nuclei with ^{3}H-Thymidine

Time with actinomycin (min)	DNA formed: C.p.m. ^{14}C mg^{-1} DNA	DNA formed: C.p.m. ^{3}H mg^{-1} DNA	^{3}H/^{14}C	% Labelled nuclei	Labelled nuclei: Grains/nucleus	Labelled nuclei: $\frac{\text{C.p.m. }^{14}\text{C mg}^{-1}\text{ DNA}}{\%\text{ labelled nuclei}}$
*	1,060	2.5×10^5	236	29	17	37
15	940	1.9×10^5	202	25	13	38
30	1,260	2.0×10^5	159	30	12	42
45	1,710	1.8×10^5	105	38	8.5	45
60	1,320	1.0×10^5	76	32	6	41

Partially hepatectomized rats were given 0.05 μCi of ^{14}C-thymidine at 22 h after the operation. After 45 min, each animal was given 0.5 mg of actinomycin and, 15 to 60 min later, 100 μCi of ^{3}H-thymidine. Liver samples, taken 60 min after the last injection, were used for autoradiography and for the estimation of the specific activities of the ^{14}C and ^{3}H-labelled DNAs. Labelled nuclei were scored in parenchymal cells only. Each value for the "grains per nucleus" is the average of the results with 200 to 400 nuclei and background was taken to be 1 grain per nucleus.

* The rat received saline solution in place of actinomycin.

Table 3 ^{3}H-TTP Incorporation by Isolated Liver Nuclei from Rats Treated with Actinomycin and Rate of Elongation of DNA Strands *in vitro*

Actinomycin	Additions (+) or omissions (−)	DNA formed (c p m mg^{-1} DNA) *in vivo*	DNA formed (c p m mg^{-1} DNA) *in vitro*	Rate of chain elongation (nucleotides min^{-1})
−	None	2,460	57,100	194
	−dATP, dCTP, dGTP		1,380	
	−ATP		7,960	
	+actinomycin (3 µg ml^{-})		35,200	126
	(10 µg ml^{-1})		20,700	65
+	None	2,090	42,600	223
	−dATP, dCTP, dGTP		1,030	
	−ATP		7,550	

Partially hepatectomized rats were labelled with 0 1 µCi of ^{14}C-thymidine at 22 h after the operation and, 45 min later, some of the animals received a saline solution and the others received 0 5 mg of actinomycin D At 60 min after the second injection, liver nuclei were isolated and incubated for 5 min or 1 min ("rate of chain elongation") in reaction mixtures containing ^{3}H-TTP[17] Rates of DNA strand growth were estimated as in Table 2 Each value is the average of the results of two experiments

Density Gradient Analyses

To explore the possibility that the RNA needed to initiate liver DNA synthesis was formed even in animals treated witn actinomycin, rats that had been given antibiotic (0 5 mg) 15 min earlier were labelled for 5 min with a mixture of ^{14}C-thymidine (1 µCi) and ^{3}H-orotate (250 µCi) Nuclear DNA was isolated, denatured by heating (80° C for 10 min) in 12% formaldehyde, and centrifuged in an equilibrium gradient of neutral CsCl No labelled RNA was detected in the area of the ^{14}C-DNA The same results were obtained with liver DNA from partially hepatectomized animals not given actinomycin

Different results were obtained when 90% formamide was used for denaturation (37° C for 30 min) In this case, DNA from partially hepatectomized rats not treated with actinomycin, showed a sharp ^{3}H peak which was slightly more dense than most of the DNA and which was made completely acid-soluble with RNase and NaOH Identical results were obtained, however, with animals with intact livers even though the level of DNA synthesis was less than 5% of that after partial hepatectomy It would seem that formamide, unlike formaldehyde, did not denature all RNA-DNA hybrid molecules Incomplete denaturation rather than covalent linkages may explain some of the positive results that have been reported with eukaryotic cells

In the conditions of the experiment using formaldehyde, the specific activity of UTP was found to be 5×10^6 c p m µmol^{-1} and, taking a value of 4 nmol mg^{-1} of liver DNA for the pool size of TTP[19], the specific activity of the deoxynucleotide was $0 5 \times 10^6$ c p m µmol^{-1} As the peak fraction of ^{14}C-DNA in the gradient contained 200 c p m, labelled RNA should have been detectable in the DNA area if the ratio of radioactive nucleotides in RNA and DNA were no lower than 1 200 A value of 1 2 or 1 4 has been found for very nascent Okazaki fragments in *Escherichia coli*

Evidence for RNA covalently linked to liver DNA was also sought by comparing the densities of nascent DNA (0 5 min labelling period with ^{3}H-thymidine) and bulk DNA from partially hepatectomized rats that had not been treated with actinomycin Equilibrium centrifugation in neutral gradients of CsCl showed that the nascent DNA had exactly the same density as most of the DNA Identical results were obtained with DNA that was extensively sheared by sonic oscillation (about 900 nucleotides)[17] before centrifugation

TTP and Deoxynucleotide Synthesis

Actinomycin (0 5 mg) depressed by about 30% the ability of the liver to convert ^{3}H-thymidine into ^{3}H-TTP at 90 min after the injection The antibiotic caused an even greater reduction in the synthesis of cytosine deoxynucleotides from cytidine Thus, at 90 min after injection of partially hepatectomized rats with a saline solution or 0 5 mg of actinomycin D, the radioactivity (c p m mg^{-1} DNA) in liver cytosine deoxynucleotides was 6,080 (range 5,500 to 6,650, three rats) and 2,040 (range 1,390 to 3,300, five rats), respectively, as measured after labelling for 5 min with 250 µCi of ^{3}H-cytidine[20] Entry of the ^{3}H-cytidine into the liver was not affected by the antibiotic as the total acid-soluble counts were the same in both groups of animals The reduced availability of labelled and unlabelled substrates for DNA synthesis may account for the decrease in thymidine uptake in the rats treated with actinomycin

No Essential Role

The results with actinomycin do not support an essential role for transcription concomitant with nuclear DNA replication in liver A level of the antibiotic that almost completely stops RNA synthesis causes only a slow decline in DNA formation The decline seems to be due to a reduction in the rate of elongation of DNA chains and not to a loss in the ability to start new chains Finally, no evidence could be found for the existence in regenerating liver of RNA covalently linked to nascent DNA

Nevertheless, the possibility cannot be ruled out that RNA molecules are required for the initiation of hepatic DNA synthesis If this is so, however, it must follow that the RNA is made by a unique polymerase that is highly resistant to actinomycin D or that all the initiating RNAs are completed before or early in the S period or that the initiating RNA, unlike that of bacteria[3], is needed only very infrequently during the replicative process The last possibility is unlikely, for even after 45 min of exposure to actinomycin, about 10% of the S period, the reduction in thymidine uptake is only 50%

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LETTERS TO NATURE

PHYSICAL SCIENCES

New Method for Direct Determination of UT1

ALTHOUGH Atomic Time is now available (for example as coordinated time, UTC) to a precision far in excess of that to which any astronomical time scale can be determined, astronomers, navigators and surveyors, concerned with their position on the rotating Earth, still require a knowledge of Universal Time, UT1 Universal Time is obtained by calculation from observed sidereal time, usually measured by timing the passage of stars across the meridian with a transit circle, or, more recently, with a photographic zenith tube This measure of Universal Time, UTO, contains irregularities due to both polar motion, sometimes known as Chandler Wobble, and variations in the rate of rotation of the Earth, and its value at any instant depends upon the position of the observer on the Earth

Of much more general use is UT1, which is the same at all locations and provides a measure of the rotation of the Earth about a pole of mean position The correction that must be applied for polar motion to derive UT1 from UTO relies upon measurements of the instantaneous position of the pole, obtainable only by combining observations of the variations of latitude made by several collaborating observatories situated at widely spaced longitudes

The method described here, based on observations of radio sources with an east-west interferometer, provides a determination of UT1 that is independent both of the proper motion of stars and of the instantaneous position of the pole and has the added advantage over all optical methods of being largely independent of weather conditions Some preliminary results are given, derived from recent measurements with the 5-km telescope at Cambridge[1]

The technique for measuring the positions of radio sources with east-west interferometers has been developed to a high precision, enabling right ascensions and declinations to be independently determined[2-4]. It will be sufficient here to outline the method of measurement of right ascension and to show how this may be applied to provide a determination of UT1

The phase difference Φ between signals at a wavelength λ arriving at two aerials of an east-west interferometer of spacing d is given by

$$\Phi=2\pi\,(d\sin H\cos\delta)/\lambda$$

where δ is the declination and H the hour angle of the source at any instant If the measured phase Φ is compared with the value Φ_0, calculated from an assumed hour angle $(H+\Delta H)$ for the source, then

$$\Phi-\Phi_0=-2\pi\,(d\,\Delta H\cos H\cos\delta)/\lambda$$

From 12 h observations made with H from −6 h to +6 h, the measurement of the component of $\Phi-\Phi_0$ varying as cos H thus provides a value for ΔH With the 5-km telescope, an on-line computer plots the results of the 12 h observations on a graph plotter, derives the best fit curve as shown in Fig 1, and prints out the corresponding value of ΔH

This difference, ΔH, between the measured and assumed values is usually interpreted so as to provide a correction to the assumed right ascension of the source, having taken due account of all aspects of timing But when the right ascension of a source has been determined, subsequent observations may be used instead to give measurements of time, provided that the overall phase of the instrument and atmosphere remains sufficiently constant during the 12 h period of observation[3]

The cabling and receiver systems of the 5-km telescope have been designed to minimize phase variations arising within the instrument, and variations arising from external causes are, in general, dominant As hour angle, and hence time, are determined from measurements of the relative phase of signals arriving at two aerials, only differences in the two ray paths are important These differences arise from the curvature of the atmosphere and ionosphere and also from dissimilar heights of aerials above the geoid Corrections for these effects are small[4] and do not vary significantly with barometric pressure Irregularities of water vapour content in the troposphere, however, produce phase variations[5,6] for which no correction is possible and which limit the overall accuracy attainable The irregularities are most pronounced during the daytime in summer but their occurrence is easy to recognize, as shown in Fig. 1*b*, and observations affected may then be given lower weight

If the assumed longitude of the radio telescope is in error, there will naturally be a corresponding timing error Somewhat surprisingly this error is, to first order, independent of polar motion, as may be seen from the following argument The instantaneous position of the pole is conventionally measured by angles from the mean position, denoting small rotations about axes through the centre of the Earth of, x, towards Greenwich, and y, at right angles to x, towards the west Departure, of the pole from its mean position in general gives rise to (i) a variation of latitude, which has no effect on the phase difference measured with an east-west interferometer, and (ii) a change in the direction of the local meridian and hence a variation of longitude Thus for an interferometer situated at latitude φ and longitude Λ west, the departure of longitude from the mean position by ΔΛ, in the sense of increasing the longitude westwards, is given by

$$\Delta\Lambda=(x\sin\Lambda-y\cos\Lambda)\tan\varphi$$

This is the expression used to derive the correction relating UT1 and UTO Finally, the displacement of the pole causes (iii) a variation of the astronomical azimuth of an interferometer

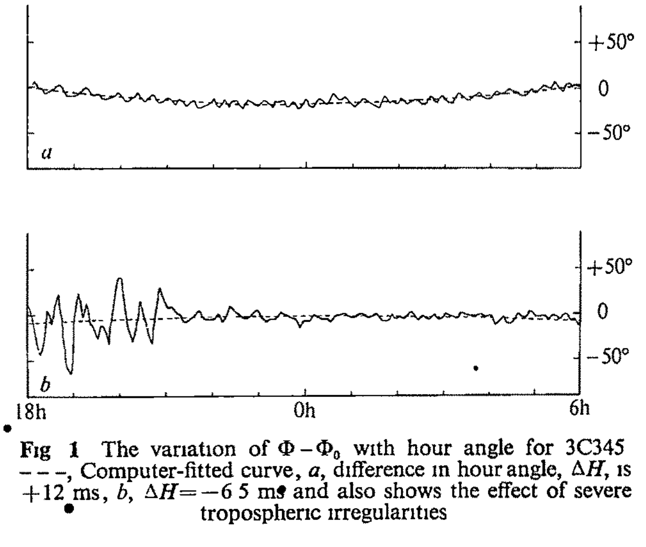

Fig 1 The variation of $\Phi-\Phi_0$ with hour angle for 3C345 – – –, Computer-fitted curve, *a*, difference in hour angle, ΔH, is +12 ms, *b*, $\Delta H=-6$ 5 ms and also shows the effect of severe tropospheric irregularities

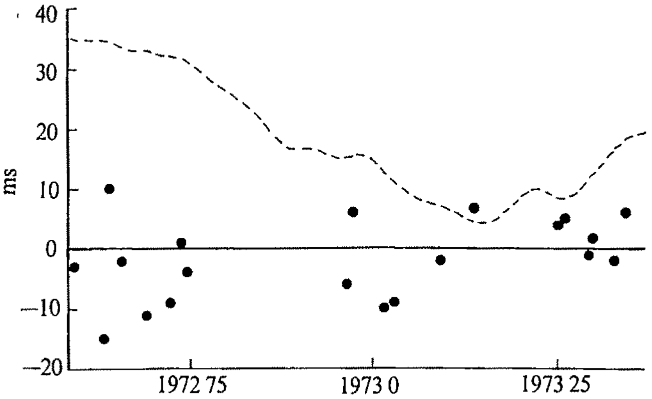

Fig. 2 ●, Differences between the measured and BIH values of (UT1−UTC), indicating the scatter in the radio measurements of UT1, ----, variation of (UT1−UTO), calculated for Cambridge.

fixed on the surface of the Earth. The change in azimuth ΔA, in the sense of decreasing the azimuth measured positive from north through east, is given by

$$\Delta A=(x \sin \Lambda - y \cos \Lambda) \sec \varphi$$

This incremental change in azimuth may be resolved into two vector components, one parallel to the polar axis and another in a plane perpendicular to the polar axis. The component along the polar axis has no influence upon hour angle, but the other component, of magnitude $\Delta A \sin \varphi$, is equivalent to an incremental change in longitude. But $\Delta A \sin \varphi = \Delta\Lambda$ and so when the combined effect of the instantaneous position of the pole is considered, producing variations of both longitude and azimuth, the net result is zero and the effective longitude of the interferometer is independent of polar motion.

To investigate the use of the 5-km telescope to derive UT1, the radio source 3C345 was observed at intervals between August 1972 and May 1973. The longitude of the telescope was determined from measurements of β Persei, thus enabling the right ascension to be established[4] relative to the FK4 fundamental catalogue[7]. The basic timing relies upon a quartz crystal clock, regulated to mean sidereal time. As the instrument is primarily used for aerial synthesis, for which it is frequently necessary to combine observations from one day to the next with the correct phase relationship, the clock is adjusted to follow UT1 closely. This is normally achieved by correcting for clock error, determined daily from the 60 kHz transmission of UTC from MSF Rugby, and by extrapolation of provisional values of UT1−UTC received weekly from the Bureau Internationale de l'Heure (BIH). The present observations have been analysed instead to give UT1−UTC independently of the data from the BIH.

The results are shown in Fig. 2, in which differences are plotted between the measured values of UT1−UTC and the corresponding values published by the BIH, thus giving a direct comparison of the two determinations of UT1 over the period. In addition, calculated values of UT1−UTO for Cambridge are indicated for comparison. There is excellent agreement between the measured and BIH values of UT1, the probable error of a single determination being ±4.6 ms, which includes the error in the BIH value. This compares favourably with the external probable error of measurement of ±18 ms from a single night's observations using a meridian circle with impersonal micrometer, and ±12 ms when photoelectric registration is employed[8]. The corresponding value for the photographic zenith tube is ±4 ms (ref. 8).

The early observations were made in daytime in summer and in consequence have larger errors than if they had been made at night with some other source. It should therefore be possible to achieve improved accuracy with the present instrument. Even more accurate measures of the rotation period of the Earth may be forthcoming from very long baseline interferometry[9] and from satellite and lunar laser ranging[10], but the technique used by the 5-km telescope provides a self contained and fully automated measurement of UT1 that has the advantage of being available immediately at the end of a 12 h observing period.

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Are the Jovian Planets "Failed" Stars?

THERE are three distinct types of object in the Solar System—the Sun is a star; the terrestrial planets (Mercury, Venus, Earth/Moon, Mars) are solid bodies; and the Jovian planets (Jupiter, Saturn, Uranus, Neptune) are cold gaseous bodies. The nature of Pluto is not established and Pluto will be discounted for my purposes here. It is surely no accident that the solid members of the planetary system lie nearer the Sun than the gaseous members. The most distant terrestrial planet (Mars) is 1.52 AU from the Sun whereas the nearest Jovian planet (Jupiter) is 5.20 AU from the Sun (1 AU=1.496×10^8 km). As yet no agreed view of planetary formation exists. Most theories involve a single process for all the planets (see, for example, ref. 1). I suggest that the division of the planetary bodies into solid and gaseous types may imply different formation mechanisms. In particular I suggest that the terrestrial planets formed in a high density shell surrounding the proto-Sun and that the Jovian planets are the remnants of other attempts to form stars contemporaneously with the Sun.

Our numerical treatment[2] of collapse under gravity for spherically symmetrical gas clouds showed that collapse under gravity takes a characteristic form, which has also been found by others[3-5].

Gravitational collapse takes place on a time scale determined by $\rho^{-\frac{1}{2}}$, where ρ is the mean initial density, in such a manner that the density increases slowly at first, but proceeds rapidly in the last 10% of the collapse time; increases of density of, say, fifteen orders of magnitude taking place in the last few per cent of the collapse time. This form of collapse means that for the collapse of two clouds differing in density by a factor of 9, while having collapse times differing only by a factor of 3, the higher density cloud will have completed its collapse to high densities before the lower density cloud will have been sufficiently compressed to increase its density by one order of magnitude. The implication of such a characteristic form of collapse is that, provided collapse can be maintained, a gas cloud, which has a monotonically decreasing density distribution from centre to boundary, will collapse such that the cloud may be considered in two parts—a rapidly collapsing small core of high density surrounded by a slowly collapsing low density

Table 1 Densities of Objects in the Solar System

Gaseous objects		Solid objects		Planetary satellites		
Object	Density*	Object	Density*	Parent planet	Object	Density*
Sun	1 409	Mercury	5 4	Earth	Moon	3 34
Jupiter	1 334	Venus	5 1	Jupiter	Io	5 0
Saturn	0 684	Earth	5 52		Europa	4 9
Uranus	1 60	Mars	3 97		Ganymede	3 0
Neptune	2 25				Callisto	2 3
				Saturn	Mimas	0 5
					Enceladus	0 8

* g cm^{-3}

envelope It is the shell joining the high density core to the low density envelope which is of interest in the context of the formation of the terrestrial planets I have drawn attention elsewhere[6,7] to the effects of the density variation, by a factor of at least 10^{15}, and temperature variation, by at least a factor of 10^3, within the shell linking core and envelope, on the rates of chemical reactions At the highest densities and temperatures in the inner parts of the shell, chemical processes will take place very rapidly, producing many molecular species[7] Aggregation of molecular species into particulate matter would also be expected Conditions are therefore appropriate for the formation of solid planets if the nature of the protostellar body is such that dispersal of the particulate matter does not take place soon after its formation, that is, conditions for proceeding to aggregation into planetary bodies may only be found for the less massive protostellar objects

Any object which had collapsed to a high density condition would be surrounded by a shell in which extensive chemical evolution had taken place and particulate matter formed One would expect that were the Jovian planets of this type some evidence of such chemical evolution would exist In the case of Jupiter and Saturn circumstantial evidence in favour of the hypothesis does exist Table 1 shows the densities of some Solar System objects[8] All the solid planets have a mean density in excess of 3 g cm^{-3} whereas the gaseous planets have a mean density of <2 g cm^{-3} (with the exception of Neptune) One might conclude that the three inner satellites of Jupiter—Io, Europa and Ganymede—could be regarded as solid bodies Saturn is surrounded by its rings of particulate matter and its nearest satellites, Mimas and Enceladus, are of very low density, comparable with the density of Saturn itself The comparison of solar mean density with that of the Jovian planets is striking The evidence, such as it is, does not conflict with the hypothesis that the Jovian planets may be remnants of other attempts to form stars

If, however, "failure" to form a star can occur, one can legitimately ask why is it possible for a star to form in some situations and not in others, more particularly as it is clear that if the Jovian planets are "failed" stars, the collapse has proceeded almost to the stellar state? What could prevent ultimate evolution to the stellar state? Clearly it is not proximity to the Sun, for some binary stars have separations of $<0\ 05$ AU Some other force or forces must be at work and may exist in the dynamics of the star formation process

The models of star formation based on gas clouds idealized to have spherical symmetry are unrealistic As the gas clouds are observed to be irregular in shape and rotating, collapse under gravity will probably lead to flattened structures As was originally demonstrated by Lin *et al*[9], a nonrotating spheroid will flatten during collapse Rotation will enhance the tendency to flatten But rotation is also seen as an inhibitor of collapse As centrifugal forces amplify as l^{-3} whereas gravity amplifies at l^{-2} during collapse, where l is a characteristic linear dimension, it is clear that even if gravity dominates centrifugal forces originally, the greater amplification of centrifugal forces will cause them eventually to dominate gravity The conditions prevailing in interstellar gas clouds suggest that centrifugal forces should halt collapse soon after it starts Much effort has been expended on mechanisms for removal of rotation of gas clouds, and the rotational problem is seen as one of the greatest difficulties encountered by any theory of star formation through collapse

Numerical studies which we are carrying out on the collapse of gas clouds in two and three dimensions have indicated that such problems may be less severe than supposed To make the problem specific, I shall consider the free-fall collapse of a uniform spheroid under gravity Such a cloud maintains its uniform density and spheroidal shape during collapse, becoming progressively more and more flattened The introduction of rotation about the minor axis of the spheroid does indeed reduce the collapse rate and may even cause equatorial expansion, but it does not prevent flattening Indeed excess rotation does not cause the cloud to break up in these conditions, but merely generates an expanding ever thinning spheroid Clearly other forces are necessary to cause breakup

The extension of the work to cover the case of collapse of rotating gas clouds under gravity when pressure cannot be neglected is not yet complete It is, however, clear that the halting of collapse by centrifugal forces acts progressively inwards as collapse proceeds The region where infall can proceed for longest is that lying close to the axis of rotation It follows that any accumulation of material at the centre of the cloud, through infall of material originally close to the minor axis, will have low angular momentum If, however, the angular momentum of the cloud is large initially the centrifugal forces may effectively disperse the infalling material Here then is a circumstance which could act at a late stage in the evolution of a gas cloud to the stellar state and inhibit actual attainment of that state The numerical studies also suggest that details of the physical state may influence the dynamics of collapse in a sensitive way Collapse once initiated may be frustrated by the interplay of many different factors and the occurrence of high density may not of itself ensure ultimate star formation

The numerical studies in which we are at present engaged demonstrate very clearly that models of star formation which assume spherical symmetry are misleading A spherically symmetric model shows no tendency to flatten Any small departure from exact spherical symmetry will lead to flattening Therefore there is no problem in producing flattened systems through collapse under gravity Rotation, far from being a difficulty, may be necessary to produce a braking of the collapse for the bulk of the gas cloud, so preventing its eventual collapse onto any protostellar objects at its centre The limitation of rate of accumulation of mass, through the imbalance of inflow near the axis of rotation of a cloud and outflow caused by centrifugal forces perpendicular to the axis of rotation, is clearly a factor controlling the growth or dispersal of accumulations of mass Rotation may therefore be an essential component of the process of star formation, acting as a restraint on gravitation As other forces are also acting on a collapsing cloud, the interaction is likely to be complex It is quite clear, however, that reliance on ideas derived from consideration of a spherically symmetrical model will lead to misconceptions in any attempt to understand the formation of stars through collapse under gravity

The collapsing region out of which the Sun eventually formed will have contained density fluctuations which will have amplified during the collapse Conditions of rotation and physical state will, however, have been such that only the density fluctuation now observed as the Sun could evolve to the stellar state, the other density fluctuations must have become inhibited and are now observed as the Jovian planets Solar System objects such as asteroids and comets were then forced to develop within the constraints imposed by the forming Sun and its solid satellites—the terrestrial planets—and the attempted star formation by the Jovian planets

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Rotation of the Earth during the 1972 Solar Event

Gribbin and Plagemann[1] have used the UT observations of the US Naval Observatory (USNO) as evidence of "a discontinuous change in the length of the day and a change in the rate of change of the length of the day" following a great solar storm in which the flare activity reached a maximum on August 4, 1972 They claim that variations in the UT observations of the USNO, soon afterwards, have confirmed their own prediction that such a storm should influence the rate of rotation of the Earth Gribbin also asserts[2] that there was a 10 ms jump in AT − UT2 between August 7 and 8 The evidence is presented in the form of graphs of AT − UT2 (UT2 values are the UT observations corrected for observed polar motion and for a seasonal variation in the rate of rotation of the Earth, using the Bureau Internationale de l'Heure (BIH) adopted corrections) The precise significance of the graphs is difficult to assess because of the irregular indexing of the axes No mention is made of the instrument or instruments on which the data are based

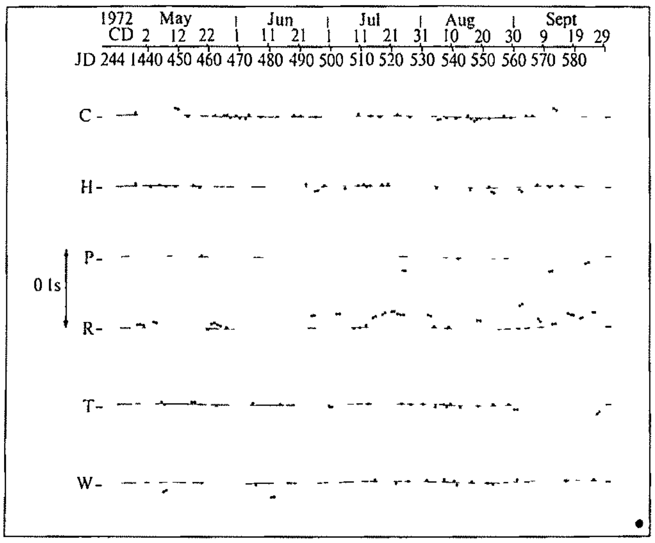

Fig 1 UT2−AT, May to September 1972 C, Calgary photographic zenith tube (PZT), H, Herstmonceux PZT, P, Paris Astrolabe, R, Richmond PZT, T, Tokyo PZ T, W, Washington PZT, ——, Def UT2—AT

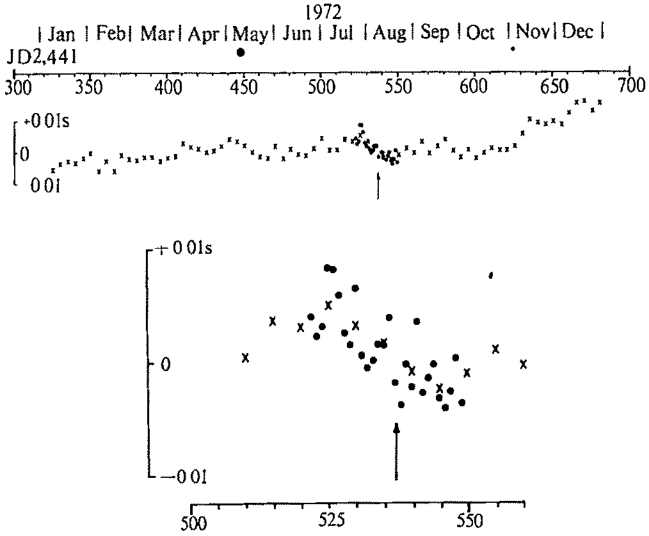

Fig. 2 UT2 − AT, BIH raw values, determined from all data and corrected for drift of −3 2 ms d^{-1} ×, 5-d values, ●, daily values

The astronomical observations of a single instrument can be systematically influenced by many factors, for example, errors in the adopted star places and instrumental or meteorological effects which can introduce an annual term in the results and random and unpredictable variations causing either a temporary wandering or an enhanced scatter Uncorroborated results of any instrument over a brief period should therefore be treated with great caution, particularly where results of a worldwide network of instruments are available The UT observations of many individual observatories are communicated weekly to the BIH where they are collated and analysed and corrected for systematic errors, and combined to establish a scale of Definitive UT (Def UT)

In Fig 1 we show the UT2 observations for individual nights during May to September 1972 of six instruments of maximum weight in the BIH scale of assessment The plotted points represent the observed values of UT2 − AT which, for convenience, have been corrected by application of a linear term $a+bt$ where $a = 10\ 3984$ s, $b = 0\ 0032$ s and t is the number of days elapsed since JD 2441429 5 During this period the run of the observations is, in general, linear Any change in the trend of the observations would indicate a change in the rate of change of the length of the day, any discontinuity a sudden change in the length of the day The dispersion in the observations is normal and the graphs illustrate how difficult it is to discern a significant change by the examination of the results of one instrument or, indeed, of the combined results of several instruments, over a few months

From the BIH Annual Report for 1972, 5-d raw values of UT2 − AT can be obtained, determined from all available data In Fig 2 we show these raw values corrected for a drift of −3 2 ms d^{-1} For the period July 24 to August 20, 1972, daily raw values of UT2 − AT have been supplied privately by the BIH An enlargement of this section of the diagram is shown immediately below the plot for the whole year August 7-8, 1972, is marked with an arrow

The data of Fig 2 demonstrate that small short-term variations frequently occur in the observed rate of rotation of the Earth, but that there was no significant change in the length of the day in August 1972, certainly nothing more remarkable than occurred several times in the year for which the data are presented and over which the nominal UT2−AT rate is $-3\cdot2$ ms d^{-1}.

The data we have examined do not support the findings of Gribbin and Plagemann. Indeed, if a solar storm of such exceptional magnitude as that of August 1972 exerted such little influence on the rate of rotation of the Earth, then there are good grounds for believing that changes in the length of the day are induced by some other mechanism.

We thank the staff of the RGO for assistance and H. M. Smith for discussions. The Paris Observatory, the Seismology Division of the Department of EMR, Ottawa, and the US Naval Observatory, Washington, provided unpublished data; the BIH and Tokyo data come from published circulars.

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The Earthquake of Managua, Nicaragua, 1972

THE earthquake occurred on December 23, 1972, at 0630 GCT. It had a magnitude $M_b = 5\cdot7$ ($M_s = 6\cdot1$) and a superficial focus of about 5 km. The epicentral region, which did not exceed in diameter more than a few kilometres, comprised the central part of the city of Managua where, out of a population of 400,000, about 10,000 were killed. The earthquake and the fire that followed caused damage to property estimated at about £120 million. A strong-motion AR-240 recorder located about 7 km from the centre of the city, at the ESSO refinery, registered maximum ground accelerations of 40%g, the duration of severe shaking was about 6 s. The principal shock was preceded by a small foreshock and followed by many aftershocks of magnitude equal to or less than $M_b = 5\cdot1$.

Historical evidence shows that during the past three centuries the region of Managua has been devastated by several local earthquakes. In 1648, 1651, 1663, 1844, 1881, 1885, 1902, 1907, 1918, 1926, as well as in 1931, Managua suffered considerable damage. Some of these earthquakes were associated with ground deformations as a result of which the flow of streams was arrested and in places permanently diverted.

In 1931 Managua had a population of 70,000, and the earthquake of March 31, 1931, killed 1,100 people in the city and caused £15 million worth of damage. Ground deformations associated with this earthquake were found running along a line trending N 25° E through the districts of La Veloz, Carmen, El Boer and Frixione (Fig. 1).

On January 4, 1968, another very shallow earthquake, magnitude $M_b = 4\cdot7$, caused ground fracturing, slumping and landslides within an area of 15 km^2, about 7 km to the south of the city. Damage was localized to Colonia Centroamericana, a suburb of Managua.

Managua has grown around the volcanic lake Tiscapa, and the city is founded on thick layers of gently dipping pyroclastic débris, lapilli and ash of high permeability with a water table at a depth of 20 to 40 m.

Apart from falls and slides of débris along steep stream banks and road cuts, the earthquake of 1972 did not cause any foundation failures or liquefaction. In general, the foundation materials in Managua are intrinsically competent and they cannot be held responsible for the damage that the city suffered. Damage was local and varied erratically over short distances. This was chiefly because, with few exceptions where design

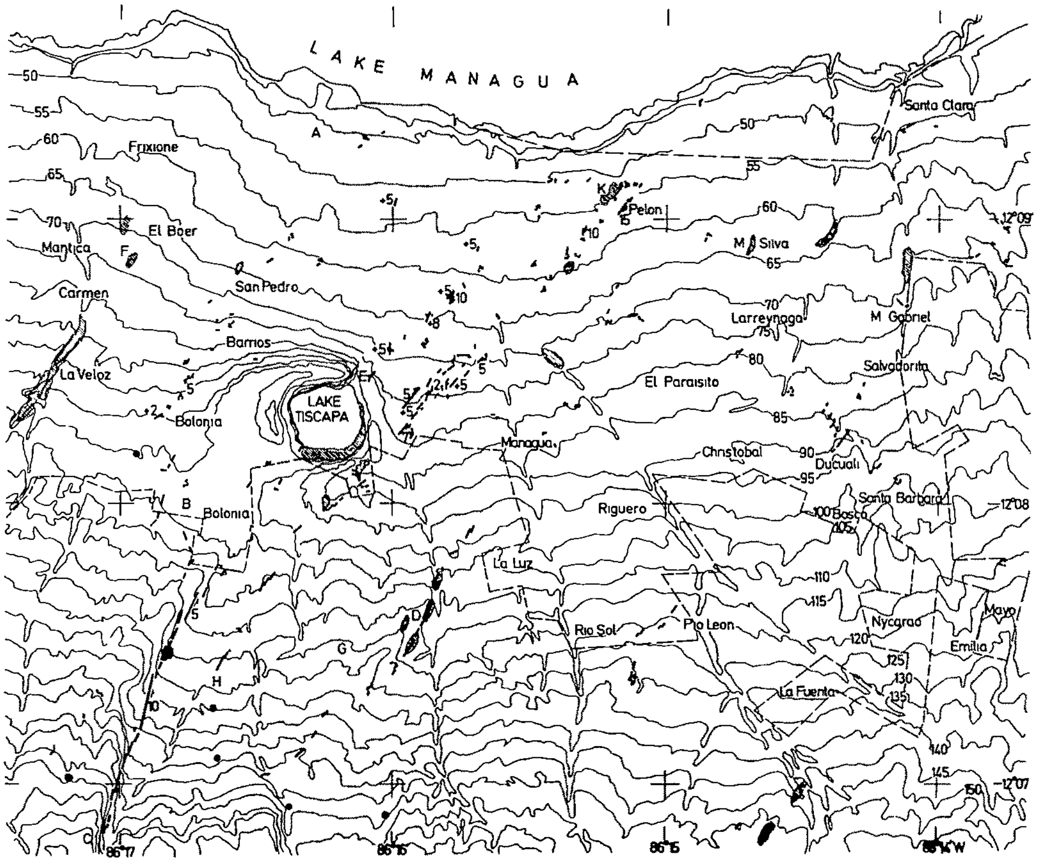

Fig. 1 Ground deformations associated with the earthquake of December 23, 1972, in Managua. Displacements in centimetres, contours in metres, shading indicates landslide and slumping areas. The city limits are shown by a thin dashed line and city districts are indicated. A, Cathedral, B, El Retiro General Hospital, C, Country Club, D, American College, E, US Embassy, F, Somoza Stadium, G, Universidad Centroamericana, H, Quinta Cecilia, K, Custom House, M, Cartographic Service.

techniques were adequate, construction was infested with bad detailing and materials In most cases modern methods of design were not followed up by equally advanced construction methods

The epicentral intensity assigned to the earthquake by various observers varies from VII to X (MM), and intensity maps, prepared by different field parties, seem to depict the distribution of the quality of building materials, methods of construction and age of buildings in the city rather than the distribution of earthquake intensity, no two samples of these maps look remotely alike

The earthquake of 1972 was associated with minor but extensive ground deformations These were found in surfaced roads, gardens and open spaces in the city as well as in the fields to the southeast of Managua A cursory study of these features shows that most offsets on individual fractures were left-lateral by as much as 15 cm and that vertical offsets displayed very small throws, mainly to the southeast and not exceeding 5 cm Individual fractures, arranged *en echelon*, did not extend uninterrupted for more than some tens of metres

In Fig 1 I show the ground fractures associated with the earthquake These fractures define a rupture zone about 6 km long and 1 5 km wide which coincides with the Tiscapa fault The cumulative lateral offset measured across this zone is at least 50 to 60 cm

Long rigid elements, such as pavements with large concrete slabs, curbs and surfaced footpaths crossing the zone at an acute angle were in places found to be humped up and shortened or stretched out by 30 to 40 cm

It is probable that this rupture zone extends northeast into Lake Managua To the southwest, minor ground deformations and landslides found to the southeast of the 6th and 9th kilometre "carretera" of the Panamericana Motorway suggest that this zone, which trends N 38° E, extends for another 6 km in that direction

This zone of fractures, about 12 km long and 1 5 to 2 0 km wide, seems to reflect the surface expression of a tectonic adjustment on the buried Tiscapa fault

There seems to have been no change in the shoreline of Lake Managua, nor is there any indication of movement on the alleged rupture zone of 1931 Slumping of the ground in and around the Somoza Stadium was due to the collapse of underground galleries belonging to the old prison that occupied the site

A detailed field study of the distribution of damage in the city, carried out by the writer on two separate occasions, shows that there was little, if any, relationship between damage due to vibrational effects and proximity to the surface ruptures

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Search for Superheavy Elements in Natural and Proton-irradiated Materials

WE have used an improved method of measuring low levels of spontaneous fission to establish limits for postulated superheavy elements in natural materials The apparatus has also been used to give an approximate measure of the rate of cosmic ray-induced fission of lead Our result for lead agrees with theoretical predictions and satisfactorily explains observations of fission events in Pb glass that had previously been attributed to superheavy element decay[1] Measurements on a lead target irradiated with 29 GeV protons were carried out as a comparison with the latest results of Marinov *et al* [2], which would have predicted 15 counts in our experiment Our sample yielded no counts

The search for superheavy elements has been stimulated by theoretical work that indicates an island of nuclear stability in the region of the double shell closure at $Z=114$, $A=298$ (refs 3 to 5) Nilsson *et al* [6] originally predicted that the total half life for $^{294}110$ might exceed 10^8 yr, with spontaneous fission as the decay mode of the superheavy or its daughter Several experimental attempts have been made to detect the spontaneous fission of superheavy elements which might still be stored in natural materials[7-10]

Our search used an ultra-low level counting scheme to detect the fission fragments from any superheavy nuclei present The fission fragments were recorded as coincidence counts in two adjoining plastic detectors The high sensitivity was achieved by the use of large areas and long exposure times, a typical sample (100 g) was counted for 3 months with a detection area of 1 m^2 The finely ground sample was spread on a perspex plate and placed next to a pair of 3 5 μm 'Kimfol' sheets (Peter S Schweitzer Division, Kimberly-Clark Corporation, Lee, Massachusetts) mounted on separate plastic frames The sample was separated from the two detector sheets by a 75 μm plastic sheet while counting was not in progress The experiment was run in the Fairport Harbor Salt Mine, 585 m below the surface, to avoid induced fissions from cosmic rays The protective sheets were withdrawn only while the sample-counter assemblies were in the mine

The 3 5 μm sheets were later etched in NaOH to develop fission tracks, which were detected by a pulse spark method[11] The position of individual tracks was measured to ±1 mm The background rate, which was due to flaws in the plastic, was 225 counts m^{-2} for a single sheet and 4×10^{-2} counts m^{-2} for two sheets in coincidence The efficiency for detecting fission fragments from a thick depleted uranium source was determined to be 16 0±1 2% Details of the sample preparation, etching, spark counting and calibration procedures will be published elsewhere

We examined samples of the chemical homologues (Pb, Hg, Pt,) of all possible superheavy elements from $Z=108$ to $Z=114$ Most were naturally occurring ores and minerals Some were industrial concentrates Finally a sample (area 1 inch square and length 2 inch) of galena irradiated by $9\ 4\times10^{17}$ protons at 29 GeV/*c*, and one sample of purified thorium chloride ($ThCl_4$) were used

Spontaneous fission fragments from uranium impurities constitute a background which contributes one fission event for a typical sample at uranium concentration of 8 8 p p m The uranium concentration in each sample was measured by using neutron-induced fission recorded on mica detectors in conjunction with uranium glass standards[12] In about half the samples the uranium was highly non-uniformly distributed and, for these, a new method of average uranium determination based on track techniques was used (F H G , J Shirck and R M W , to be published) The thorium sample was measured spectrophotometrically[13] because fast neutron fission of thorium caused a large interference reaction The thallium mine tailings and the thorium were unacceptably high in uranium These samples were sent to Dr Johann Korkisch of the University of Vienna, who lowered the uranium concentration by an ion-exchange process

Although there were minor variations among samples, most were activated for 3 months with an area of 1 m^2 Of the forty samples exposed deep underground thirty detected no fission events, eight detected one, and one each detected three and five As a single track in any sample can be attributed to flaws in the plastic, and as the samples giving the high counts had an appropriate concentration of uranium, we consider that we have no evidence for the existence of a superheavy element

Using an assumed half life of 10^9 yr, we conclude that for a typical sample the concentration of superheavy elements is $<7\ 6\times10^{-13}$, $<4\ 5\times10^{-13}$ or $<2\ 9\times10^{-13}$ relative to the heavy homologue, assuming the range of the fission fragments is the same as for uranium[14], or increased as predicted for symmetric fission or for asymmetric fission, respectively[15]

The negative result of the superheavy search also implies that the half lives of Pb, Hg, and Th against spontaneous fission are $>3\ 8\times10^{22}$ yr, $>3\ 6\times10^{24}$ yr, and $>2\ 4\times10^{20}$ yr respectively

A galena (PbS) sample irradiated with $9\ 4\times10^{17}$ protons at 29 GeV some 11 months before the start of counting recorded no spontaneous fission events If the production rate of superheavy elements is the same for a PbS target as originally reported by Marinov *et al* [16] for a tungsten target, some fifty-one events would have been expected Our negative result supports the later work of Marinov and others[2,17 18] The null count for the proton irradiation also sets an upper limit of 3 6 pbarn for the production of ^{252}Cf by the impact of 29 GeV/*c* protons on PbS

The fission rate of galena was measured as $6\ 4\pm5\ 3$ and $9\ 6\pm6\ 7$ fissions g^{-1} yr^{-1} at the surface in St Louis and at 200 g cm^{-2} below ground respectively The expected induced fission rate computed using a calculated cosmic ray-induced atmospheric neutron spectrum given by Hess *et al* [20], corrected for the latitude of St Louis[21], and using energy-dependent fission cross sections given by Axmann *et al* [22] is 12 fissions g^{-1} yr^{-1} for lead, in agreement with our experimental results

Our value for the cosmic ray production rate is in agreement with that recently measured by G N Flerov, V P Perelygin and O Otgonsuren (unpublished) and supports their contention that fossil fission tracks in ancient Pb glasses should be attributed to the effect of cosmic rays

Our results imply either that the production rate of superheavy elements by normal r-process mechanisms is more difficult than calculated by Schramm and Fowler[23] or that the lifetimes are shorter than 10^8 yr Although, of course, we may have looked in the wrong materials, it seems likely that a more fruitful approach to the search for superheavy elements lies in studies of heavy ion reactions in targets with high atomic numbers

We thank Claude Phillips, Bernice Franklin, and Andy Taube for their help with the low level counting scheme, Jim Boyle for discussions, Jerry Schlapper for the neutron irradiation of the samples, the Morton Salt Company for the use of the mine, and Matthey-Bishop, Inc, for the loan of a platinum sample This work was supported by the National Science Foundation

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Search for Superheavy Elements and Actinides Produced by Secondary Reactions in a Tungsten Target

WE have presented evidence[1] for the possible existence of a superheavy element with atomic number 112 This evidence came principally from the observation of spontaneous fission activity in a mercury source separated from a tungsten target which had been irradiated by 24 GeV protons It was subsequently shown[2] that at a later stage 70% of the fission activity was due to ^{252}Cf The origin of the remaining 30% of the fission activity was unexplained, however, although measurements of the activity made when the source was first produced indicated that it could not then have been due to ^{252}Cf

Our previous results were based on experiments performed with three different targets identified as W1, W2 and W3 respectively Since then experiments have been carried out with two other targets, W4 and W5, and the results from these will be described As our previous evidence was based on the possible production of eka-Hg, the chief aim of the present experiments has been to separate eka-Hg from the tungsten target As well as looking for possible superheavy elements a search was also made for actinides, both as a group and individually, in order to test the possible reaction mechanism A summary of the target irradiations is given in Table 1

Table 1 Summary of Target Irradiations

	Weight of W rod (g)	Proton dose	No of ^{148}Gd atoms produced
W1	33	2×10^{18}*	
W2	33	7×10^{17}*	6×10^{15}‡
W3	36§	1×10^{18}*	
W4	45	$9\ 1\times10^{17}$†	$1\ 0\times10^{16}$‡
W5	45	$6\ 7\times10^{17}$†	$7\ 6\times10^{15}$‡

* External beam monitor value, provided by CERN Estimated error ±20%

† ^{22}Na used as an internal monitor, assuming a formation cross-section of 1 6 mbarn (refs 7 and 8)

‡ Calculation based on the measured formation cross-section of ^{148}Gd (29±4 mbarn) (ref 7)

§ The target was different from all others in that it was heavily oxidized to WO_3 (~28%)

The chemical separations carried out on the tungsten targets are described in detail elsewhere[3] For the W4 target a Pt cathode and an excess of NaOH was used in the anodic dissolution vessel A large fraction (20% to 95%) of the heavy metals (Os and Pb) was deposited as a thin layer on the cathode[3] This was kept at liquid nitrogen temperature and counted for spontaneous fission events over a 9-d period using polycarbonate plastic detectors No events were observed Later experiments showed, however, that elementary Hg deposited on the cathode was lost at a rate of 50% a week even at liquid nitrogen temperature. Because eka-Hg is likely to be more volatile than Hg this experiment cannot be considered conclusive For possible future experiments we should note that counting the cathode for spontaneous fission events could be a useful way of searching for other less volatile superheavy elements This technique involves a minimum of chemical separation and is therefore less likely to cause the loss of the wanted activity or to introduce contamination

For the W5 target a Mo cathode was used with stoichiometric amounts of NaOH in the dissolution vessel[3] To prevent loss by evaporation, the activity on the cathode was removed immediately by reverse electrolysis[3] Following chemical separation, the Hg source was made by exchange on a thin PbS film

For both the W4 and W5 targets the separation of the actinide and lanthanide elements as a group was carried out in the conventional way using F^- and OH^- precipitations and anion exchange The individual actinides from the W5 target were separated by the use of reverse phase partition chromatography using radioactive lanthanide isotopes to calibrate the column[3]. The sources were prepared electrolytically using stainless steel disks as cathodes More than 95% of the transplutonium actinides were deposited in this way[4]

Both the actinide sources and those of the elements Os to Pb from the W5 target were counted for spontaneous fission activity with polycarbonate plastic detectors but no such events were observed in 2 weeks, on the assumption that the superheavy elements decay by this mode with a half life of 1 yr the upper limit for their formation cross-section is 10^{-18} barn

Alpha activity was measured using surface barrier detectors for varying periods from days to several weeks No known transplutonium elements were observed in the actinide sources Most of the alpha peaks found in the other sources were probably due to known isotopes such as ^{148}Gd, ^{210}Po and members of the ^{228}Th decay chain

Before comparing these results with those obtained from the earlier targets, the following changes in the chemical separation should be mentioned In the present work NiS was used as a coprecipitant instead of MnO_2 because it was found to give higher and more reproducible yields of the elements Os to Pb 'Dowex' 50 was used rather than 'Dowex' 1 to facilitate the separation of eka-Hg from thorium and lanthanide contamination It is, of course, not certain that the eka element will follow its homologue in the initial or modified chemical procedures, and it is always possible that this could be the reason for the negative results of W5 This same argument also applies when comparing our work with that of other groups who have carried out similar experiments but using a different chemical approach (refs 5 and 6 and Yu A Batusov, Ts. Vylov, V P Trelov *et al*)

For the actinides the comparison can be made more easily as the chemistry of this group of elements is well established Our results are in agreement with those of Unik *et al*[5], Westgaard *et al*[6], and Batusov *et al* (unpublished) We now believe that the alpha activity previously observed in our actinide sources from W1 and W2 was largely due to contamination These findings imply that the production of energetic fragments with $Z>22$ to give secondary reactions in a tungsten target must be less than 3×10^{-15} barn (Calculations were based on production of ^{242}Cm) In the case of uranium targets irradiated with 10 to 28 GeV protons, only reaction products with atomic numbers up to 6 greater than that of the target material were found[8]

We are, however, still unable to explain the origin of the fission activity observed in the Hg source produced from the early W2 target If the spontaneous fission activity had been due to ^{252}Cf then at least 30 counts d^{-1} would have been seen in the alpha particle spectra at an energy of 6 1 MeV In fact, as can be seen from Fig 1*a* and *b* of ref 1, less than 12 counts were observed in this energy region in 27 d Similarly, measurements of the alpha/fission ratio made using a single surface barrier detector gave an upper limit of 5 1 We have recently reanalysed this data and can find no explanation in terms of ^{252}Cf or other known actinide isotopes The origin of the fission events observed in the early stages of the W2 experiment remains unexplained

In conclusion this experiment shows that we are unable to repeat the results obtained in the experiment of ref 1 We do not observe any significant production of actinides, in agreement with other work, indicating that the secondary reaction process is unlikely to be a useful way of producing superheavy elements We believe that future experiments must rely on direct heavy ion reactions

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Nature of "Anomalous Water"

MANY experiments have corroborated the phenomenon involving the formation of condensates with anomalous properties from the vapours of water and other liquids on silicate surfaces. But the nature of this phenomenon remained obscure for a long time and widely differing hypotheses were put forward to clarify it, one of them involving the formation of stable associates of water molecules $(H_2O)_n$ This hypothesis was first formulated by us[1-4] and was developed further by Lippincott *et al*[5,6].

The principal argument in favour of this hypothesis was that the contact of liquid water with the same surface does not modify its properties appreciably That is why it seemed impossible to explain that effect in terms of the simple dissolution of substrate or dissolution of the surface impurities. The "polywater" hypothesis seemed also to be corroborated by the results of primary analytical investigations that failed to detect impurity elements in it[6-8]

An alternative hypothesis attributed the anomalous properties of condensates to the effect of soluble impurity compounds detected experimentally during subsequent investigations Yet there was no consistent opinion, either with regard to the mechanism of their getting into the condensate or with regard to their respective compositions This resulted both from differing conditions in various laboratories producing "anomalous water" and from the technical difficulties involved in the analysis of extremely small amounts of a substance[9-13].

We have succeeded only quite recently in overcoming these difficulties and achieving fairly convincing results First, in collaboration with V I Spitsin and his co-workers, we used a neutron activation analysis method[14] to detect an increased concentration of sodium and silicon atoms in the anomalous water samples Then we used an electron probe method[15] to carry out investigations that were accompanied by an estimation of the layer thickness of a substance being analysed[16] This was needed to exclude errors due to the incomplete absorption of electrons by a sample under examination Samples of "anomalous condensates" as produced by many different methods were examined

We have established that there are no condensates both free of impurity atoms and simultaneously exhibiting anomalous properties Consequently, these properties should be attributed to impurities rather than to the existence of polymeric water molecules In all probability, the anomalous component is in general a mixture of silicic acid colloidal particles and molecular-dissolved compounds of Na, Si, O, C, K, Cl, and S The particles of a sol converting itself on evaporation in a gel impart increased viscosity, density, and refractive index to anomalous condensates

The molecular-dissolved compounds reduce both the vapour pressure of a solvent and its melting point The chief part of the anomalous condensate is amorphous, sometimes containing small amounts of KCl and NaCl in crystalline form[17] When produced in quartz capillaries under the cleanest conditions attainable, the samples chiefly contain O, Si, and Na This may be explained by the enrichment of quartz surface layers with sodium impurities when drawing out the capillaries An increase in the sodium concentration in the condensate may help to enhance the solubility of quartz Yet, when introducing liquid water into similar capillaries, the amount of silicon and sodium atoms dissolved was always found to be much smaller This indicates that the dissolving power of freshly condensed water is higher

Attempts to produce typical anomalous condensates on a thoroughly washed, polished surface of quartz (not enriched with sodium) have failed Experiments were carried out *in vacuo*, and a vapour stream in the form of a molecular beam scanned an area of 25 mm^2, creating an abrupt change in the vapour pressure at each point The matter washed off from the working area contained only silicon and oxygen in the same relative proportions as found in the standard silicic acid gel An aqueous solution of that substance exhibited only some of the characteristic properties of anomalous water (high density, refractive index and viscosity, for example) Hence, a pulsing vapour pressure and periodic condensation serve to increase the colloidal dissolution of quartz

In the case of samples not obtained under strictly "sterile" conditions, the presence of atoms of K, C, Cl and S may rather be attributed to the surface diffusion of impurities from an ambient medium Rousseau[18] proved that this mechanism can increase the content of impurities in condensates

Consequently, the anomalous properties of condensates may be explained, not by the formation of a new modification o water, as was previously supposed, but by the peculiar features of a reaction taking place between the vapour and solid surfaces in the process of condensation Many aspects of the mechanism of formation of anomalous condensates have not yet been fully clarified This especially applies to the formation of anomalous condensate on MgO surfaces[19,20] Only the general features of the phenomenon are clear as yet, thorough investigation by those studying processes involving the interaction of vapours and solid surfaces is clearly required

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Second Law of Thermodynamics

Wilkie[1] has recently proposed a statement of the Second Law of Thermodynamics which he implies is both new and simple

"The only processes that can happen spontaneously are those that can in principle be made to yield work, for example, to lift up a weight "

In fact this is not original, nor is it a statement of the Second Law A similar but more extensive statement, made more meaningful by an additional sentence, was put forward in a book some years ago by J A V Butler[2]

"Spontaneous processes (that is, the processes which may occur of their own accord) are those which when carried out under proper conditions, can be made to do work " Butler then adds, "If carried out reversibly they will yield a maximum amount of work, in the natural irreversible way the maximum work is never obtained "

Butler uses the first sentence merely to define "spontaneous processes" and the second to place a limitation on the work Thus Wilkie's statement is original only in that it lacks the additional sentence All it says is that something that is happening can be made to do useful work

If a statement of the Second Law of Thermodynamics is to be both a proper and useful alternative to the conventionally accepted statements it must satisfy two requirements First, it must possess the universality of the conventional statements, otherwise it is not a statement of the law and second it must lead to the usual criteria of equilibrium and all of the thermodynamic relationships which follow from the conventional statements

Wilkie's statement is lacking in both of these requirements Clearly, no attempt has been made to show how the criteria of equilibrium, and all the thermodynamic relationships, follow from it, indeed it is difficult to see how this can be done without at least an additional sentence similar to that of Butler

The most serious criticism of Wilkie's restatement of the Second Law is, however, in respect of the first condition mentioned above, that is, the question of its universality One may quote Planck[3] as an authority here After defining entropy and indicating how to measure entropy changes (parts of the statement of the Second Law), Planck states

"*Every physical or chemical process in nature takes place in such a way as to increase the sum of the entropies of all the bodies taking part in the process In the limit, that is, for reversible processes, the sum of the entropies remains unchanged* This is the most general statement of the Second Law of Thermodynamics It should be emphasized, however, that the form here given is the only one of unrestricted applicability to any finite process, and that no other universal measure of the irreversibility of the processes exists than the amount of the increase of the entropy to which they lead All other forms of the Second Law are either applicable to infinitesimal changes only, or presuppose, when extended to finite changes, the existence of some special conditions imposed on the process "

Now Wilkie proposes a "general proof" that the accepted criterion of spontaneity, $\Delta S_{cr}>0$, is the same as his criterion that the system be capable of performing work In support of his claim he uses the equation

$$\Delta S_{cr}=(W_{max}-W)/T_e$$

which purports to relate generally the entropy created as a result of a change in a non-isolated system contained in an environment at temperature T_e to the work actually obtained, W, and the maximum work possible, W_{max} Such an equation is not general and at best applies only if the temperature of the environment is constant (if indeed it is ever true for other than the trivial case for which the temperature T_e of the environment is equal to the temperature T of the system throughout the process) Moreover, the derivation of the equation, whatever the conditions for which it is valid, must begin from a conventional statement of the Second Law

Thus all that Wilkie has shown is that, in the special case of a process in a large constant temperature environment, his statement is contained within the conventional statement of the Second Law (which we note says more than just that $\Delta S_{cr}>0$ for a spontaneous process) Wilkie has not shown that the conventional statement is contained within his and hence it does not follow that the two statements are equivalent Indeed, Planck (ref 3, page 104) comments

"The amount of 'lost work' yields a no more definite general measure of irreversibility than does that of 'dissipated energy' This is possible only in the case of isothermal processes "

Wilkie's statement further lacks universality in that it cannot deal with processes in isolated systems Clearly, an irreversible process in such a system can, by definition, do no work In an attempt to circumvent this difficulty Wilkie states "this argument can be extended to an isolated system in that case the work resulting from the spontaneous change must be stored as such within the system" Now work is a mode of transfer of energy[4] and it is meaningless to claim that a mode of transfer of energy can be stored as such within the system It could possibly be argued that a process occurring in an isolated system could cause the temperature inside the isolated enclosure to increase and that "work" is thereby stored until the system is broken into and the temperature difference between the inside and outside of the enclosure used to do work Even this loose usage does not, however, lead to generality For example, consider two different perfect gases, capable of forming a perfect gas mixture, both at the same temperature and pressure but separated by a partition in a thermally and mechanically isolated enclosure When the partition is removed the gases spontaneously mix to give a final state in which the total pressure, volume, temperature and internal energy are unchanged It would be interesting to know how the work is stored in the final state of this isolated system

In conclusion, Wilkie's statement of the Second Law of Thermodynamics is not original, lacks generality, is inapplicable to isolated systems and has not been shown to lead to the usual thermodynamic relationships It is clearly unacceptable as an alternative to the conventional statements

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BIOLOGICAL SCIENCES

Inhibition of Rat Liver RNA Synthesis by Aflatoxin B1

THE administration to rats of aflatoxin B_1, a potent hepatotoxin and carcinogen, rapidly results in an inhibition of both hepatic RNA synthesis *in vivo*[1] and Mg^{2+} and $Mn^{2+}-(NH_4)_2SO_4$ stimulated RNA polymerase activities, assayed *in vitro*[2,3] Previous work has demonstrated that the RNA polymerase enzyme, isolated from hepatic nuclei whose *in situ* polymerase activity was inhibited by previous administration of aflatoxin B_1 to the animals, has an activity equal to that of enzyme isolated from control tissues[3,4] The enzyme was solubilized by incubating the nuclei in a low-salt medium, which predominantly extracts the nucleolar polymerase enzyme We have now carried out further experiments using the more vigorous technique of ultrasonication in a high-salt medium[5] which solubilizes both the nucleolar and nucleoplasmic enzymes, and have separated the enzymes by gel filtration[6]

Table 1 shows that, whereas both the Mg^{2+} and $Mn^{2+}-(NH_4)_2SO_4$-stimulated polymerase activities present in intact nuclei are strongly inhibited by the *in vivo* administration of aflatoxin B_1, the polymerase enzymes extracted by the high-salt technique retain the full activity of the nucleolar enzyme Like Saunders *et al*[7], we observed a decrease in the activity of the unfractionated enzyme extract assayed in the presence of $Mn^{2+}-(NH_4)_2SO_4$, which was reflected in a decrease in activity of the nucleoplasmic enzyme peak eluted from the DEAE-'Sephadex' column (Fig 1) In contrast to the results of Saunders *et al*[7] the percentage inhibition of the isolated nucleoplasmic enzyme was consistently less than that of the $Mn^{2+}-(NH_4)_2SO_4$ stimulated *in situ* polymerase activity (Table 1) The decreased activity of the nucleoplasmic enzyme was not accompanied by any quantitative changes in the relative activities of the enzyme when Mn^{2+} or Mg^{2+} were present as cofactors nor in the stimulation of activity which resulted from the addition of ammonium sulphate (Table 2) The dependence of the activity of the enzymes on the concentration of divalent cations in the assay medium was also unchanged (Fig 2) This situation resembles the action of α-amanitin on RNA synthesis

To explain the action of α-amanitin it has been suggested that a product of the nucleoplasmic polymerase activity regulates the synthesis of another RNA species, either directly through the RNA it produces or indirectly through a protein formed by the translation of a fraction of the RNA produced[8] Certain differences exist, however, between the

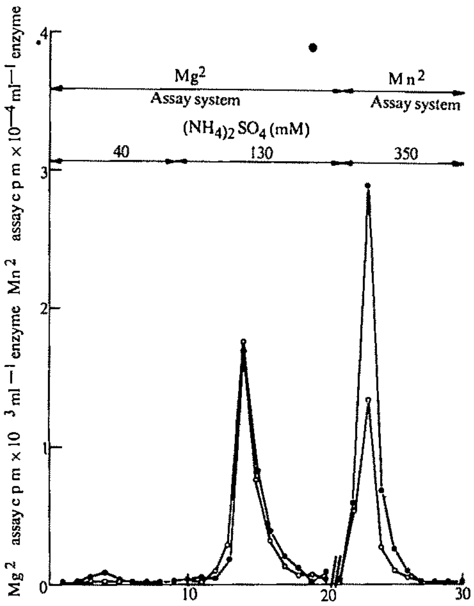

Fig. 1 Fractionation of nucleolar and nucleoplasmic polymerase enzymes on DEAE-'Sephadex' 6 68 mg protein placed on a DEAE-'Sephadex' column (2 × 3 25 cm) eluted with TGMED solution, first 27 ml containing 40 mM $(NH_4)_2SO_4$, followed by 27 ml containing 135 mM $(NH_4)_2SO_4$ then 36 ml containing 350 mM $(NH_4)_2SO_4$ 3 ml fractions were collected Assays were carried out as in Table 1 Enzymes prepared from 16 g pooled liver from groups of 5 male Fischer rats, average wt 100 g One group was injected with aflatoxin B_1 (10 mg kg^{-1}) in dimethylsulphoxide The other groups received the vehicle alone Rats were killed 2 h after injection ●, Control, ○, aflatoxin treated

actions of α-amanitin and aflatoxin B_1 which render such an explanation unlikely in the case of the latter α-Amanitin has a marked differential inhibitory action on the activities of the Mg^{2+} and Mn^{2+} ammonium sulphate polymerases in intact nuclei (20% maximum inhibition compared with 70%)[8] whereas aflatoxin B_1 has an equal effect on the two activities The rapid (<5 min) effect of aflatoxin B_1 on nuclear polymerase activity, affecting both polymerase activities equally[3], does not suggest that inhibition of the Mg^{2+} stimulated activity depends on a previous inhibition of the $Mn^{2+}-(NH_4)_2SO_4$ stimulated activity It seems, therefore, that inhibition of RNA synthesis by aflatoxin B_1 and α-amanitin, although superficially similar, depends on different underlying mechanisms, and that a better comparison for the action of aflatoxin B_1 is actinomycin, which inhibits both Mg^{2+} and $Mn^{2+}-(NH_4)_2SO_4$ activated polymerase through an action on the template mechanism Supporting this explanation is the rapid effect of both aflatoxin B_1 and actinomycin on nucleolar morphology which has been found to be temporally associated with the inhibition of rRNA synthesis *in vivo*[2] We have examined the effect of *in vivo* treatment with aflatoxin B_1 on the template capacity of rat liver chromatin and DNA, and the inhibition of the template capacities of chromatin and native DNA can be seen from the results given in Table 3 The reduction in inhibition upon heat denaturing the DNA (Table 3) could presumably be due either to the removal of the inhibitory substance by heating or to the increased availability of initiation points due to the denaturing process

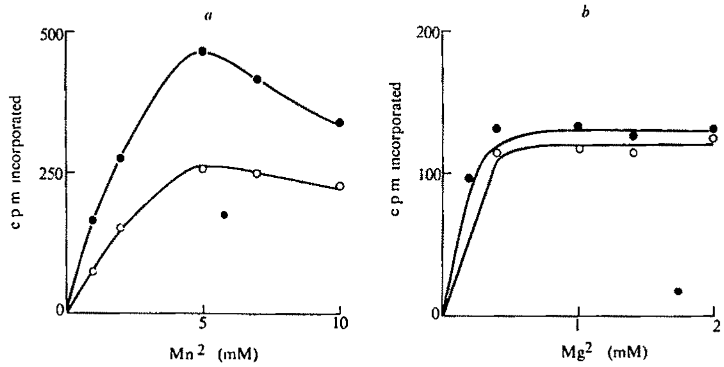

Fig. 2 *a*, Dependence of nucleolar polymerase enzyme, isolated from control and aflatoxin B_1 treated rats, on Mg^{2+} concentrations Assay conditions as in Table 1 ●, Control enzyme, ○, enzyme from aflatoxin B_1 treated animals 2 h before killing Enzyme fractions 11 to 14 (Fig 1) combined *b*, Dependence of nucleoplasmic enzyme, isolated from control and aflatoxin B_1 treated rats, on Mn^{2+} concentration Assay conditions as in Table 1 ●, Control enzyme, ○, enzyme from aflatoxin B_1 treated animals 2 h before killing Enzyme fractions 21 to 24 (Fig 1) combined

The failure of aflatoxin B_1 to inhibit the template capacity of DNA (or the activity of the polymerase enzymes) when added to *in vitro* systems may be due to a requirement for metabolic conversion of the aflatoxin B_1 to a reactive product The microsomal fraction of rat liver homogenates has

Table 1 The Effect of Aflatoxin B_1 on RNA Polymerase Activity

	Assay medium	Treatment	Polymerase activity C p m incorporated per mg DNA ± s e	B_1 treated as % of dimethylsulphoxide controls
Intact nuclei	Mg^{2+}	Dimethylsulphoxide	5,657 ± 90	
		B_1	1,219 ± 118	22
	$Mn^{2+}-(NH_4)_2SO_4$	Dimethylsulphoxide	8,074 ± 333	
		B_1	1,817 ± 72	23
			C p m incorporated per 50 μl enzyme (134 μg protein)	
Unfractionated solubilized enzyme	Mg^{2+}	Dimethylsulphoxide	549 ± 5	
		B_1	594 ± 12	108
	$Mn^{2+}-(NH_4)_2SO_4$	Dimethylsulphoxide	913 ± 64	
		B_1	397 ± 10	43

Assay conditions for intact nuclei, Mg^{2+} 50 μmol Tris-HCl, *p*H 8 5, 2 5 μmol $MgCl_2$, 10 μmol cysteine, 3 μmol NaF, 30 μmol ATP, CTP, GTP, 20 nmol ^3H-UTP (0 5 μCi), 15 min incubation at 37° C, for $Mn^{2+}-(NH_4)_2SO_4$ 50 μmol Tris-HCl, *p*H 7 5, 2 μmol $MnCl_2$, 0 5 M $(NH_4)_2SO_4$ Nucleotides as in Mg^{2+}, 10 min incubation in the absence of nucleotides, followed by 30 min incubation in the presence of nucleotides Solubilized enzyme, Mg^{2+} 50 μl enzyme in TGMED (50 mM Tris-HCl, *p*H 8, 25% v/v glycerol, 5 mM $MgCl_2$, 0 1 mM EDTA, 0 5 mM dithiothreitol), 50 μg highly polymerized calf thymus DNA, 40 μmol Tris-HCl, *p*H 8 0, 2 μmol NaF, 2 5 μmol dithiothreitol, 5 mM $MgCl_2$ Nucleotides as above, 30 min incubation $Mn^{2+}-(NH_4)_2SO_4$ 50 μl enzyme in TGMED, 50 μg heat-denatured calf thymus DNA, 40 μmol Tris-HCl, *p*H 8 0, 2 μmol NaF, 2 5 μmol dithiothreitol, 1 0 mM $MnCl_2$, 88 mM $(NH_4)_2SO_4$ Nucleotides as above, 30 min incubation Animals and injections as in Table 3

Table 2 Comparison of Cofactor Requirements of Nucleoplasmic Enzymes Isolated from Livers of Control and Aflatoxin B_1 Treated Rats

	RNA polymerase activity c p m per 200 μl enzyme		Mg^{2+}/Mn^{2+} × 100
Undialysed	Mg^{2+}	Mn^{2+}	
Control	165 ± 8	1,188 ± 49	14%
Aflatoxin	115 ± 4	569 ± 20	20%
			$\frac{+(NH_4)_2SO_4}{-(NH_4)_2SO_4} \times 100$
Dialysed	$-(NH_4)_2SO_4$	$+(NH_4)_2SO_4$	
Control	406 ± 23	635 ± 22	156%
Aflatoxin	168 ± 6	271 ± 5	161%

Enzymes prepared as in Fig 1 Assay conditions for undialysed enzyme assays, Mg^{2+} and Mn^{2+} cofactors as in isolated enzyme assays in Table 1 except $(NH_4)_2SO_4$ concentration 88 nM in both Mg^{2+} and Mn^{2+} assays Dialysed enzyme assays, nucleoplasmic enzyme after elution from column with 350 mM ammonium sulphate (Fig 1) dialysed overnight against 11 TGMED to remove ammonium sulphate Assays carried out with Mn^{2+} as in isolated enzyme assays in' Table 1 Assays with $(NH_4)_2SO_4$ contained in addition 88 mM $(NH_4)_2SO_4$

been shown to possess aflatoxin B_1-metabolizing activity[9] We have examined the metabolism of aflatoxin B_1 by rat microsomal systems and in common with other workers[9,10] have found that hydroxylation to aflatoxin M_1 represents a major route From previous studies, however, it would seem that hydroxylation is not the significant pathway in terms of the inhibition of RNA synthesis Activation of the liver drug metabolizing systems by pre-treating the animals with phenobarbitone, in spite of increasing the overall metabolism of aflatoxin B_1 and the formation of aflatoxin M_1[9], results in a decreased inhibitory effect of the toxin

Table 3 Effect of Aflatoxin B_1 Administered *in vivo* on RNA Polymerase Activity of Intact Hepatic Nuclei and Template Activity of Chromatin and DNA

Intact nuclei		C p m incorporated per mg DNA	B_1 treated as a % of dimethylsulphoxide controls
Mg^{2+}	Control	3,170 ± 287	
	B_1	1,035 ± 94	33%
Mn^{2+}	Control	6,073 ± 423	
	B_1	1,929 ± 190	32%
Nucleoplasmic enzyme		C p m Incorporated per ml nucleoplasmic enzyme	
Chromatin	Control	940 ± 40	
	B_1	380 ± 30	40%
Double stranded DNA	Control	5,110 ± 150	
	B_1	2,950 ± 90	58%
	Calf thymus	4,400 ± 40	
Heat denatured DNA	Control	10,750 ± 240	
	B_1	9,740 ± 210	91%
	Calf thymus	9,600 ± 200	

Two groups of male Fischer rats, 50 to 75 g, were used One group was given aflatoxin B_1 10 mg kg^{-1} in dimethylsulphoxide intraperitoneally and the other group received vehicle alone They were killed 2 h later, the nuclei isolated[3] and chromatin[14] and DNA[15] prepared Nucleoplasmic enzyme was prepared from control animals as in Fig 1 Assay conditions of intact nuclei are Mg^{2+} assay as in Table 1 Chromatin primed assays contained 35 μg DNA DNA primed assays contained 20 μg DNA Incorporation in absence of added primer (< 50 c p m) subtracted from results Results are means of at least triplicate assays of duplicate samples ± s e Assays were primed with 20 μg calf thymus DNA included for comparison

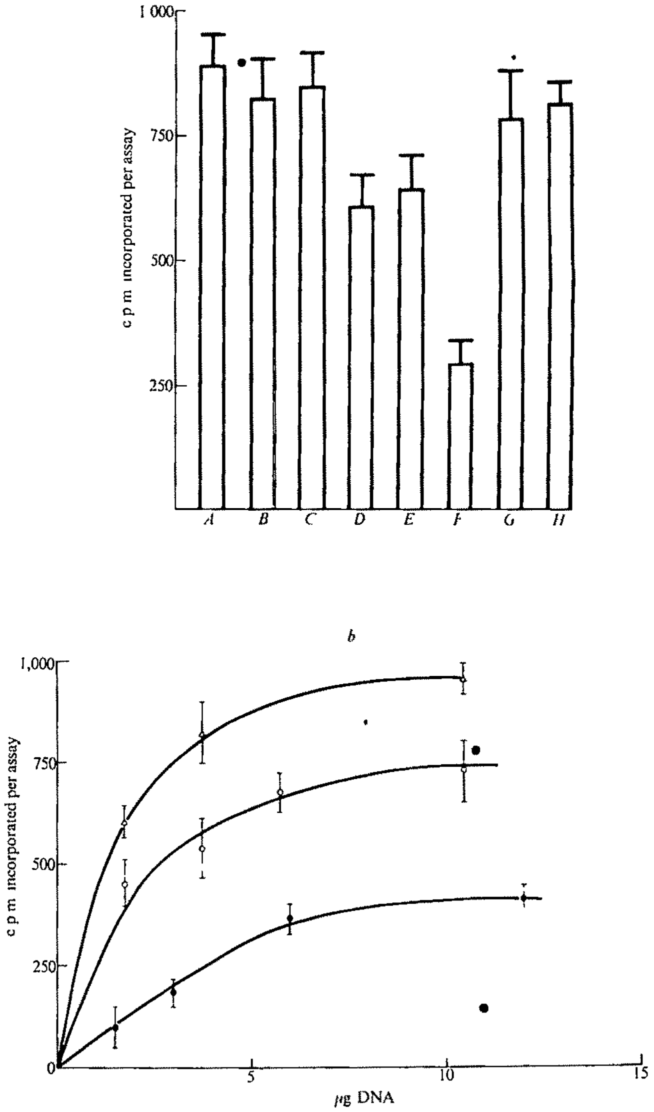

Fig. 3 *a*, Effect of microsomal metabolism of aflatoxin B_1 on the template capacity of DNA Washed microsomes were prepared by the method of Omura and Santo[16] Complete microsomal incubations (4 ml) contained 6 mg microsomal protein, 0 25 mM NAD, 0 22 mM NADP, 4 mM glucose-6-phosphate, 5 μg glucose-6-phosphate dehydrogenase, 1 mg highly polymerized calf thymus DNA, 50 μg aflatoxin B_1, 50 μl dimethylsulphoxide, 10 mM Tris-HCl, *p*H 8 0 Incubation was in the dark for 15 min at 37° C in a shaking water bath After incubation they were centrifuged at 100,000*g* for 1 h Supernatant was removed and DNA precipitated by adding the supernatant to 1 ml ice-cold spermine solution (15 mg ml^{-1}) DNA spooled onto fine glass rods, blotted, and redissolved in 3 ml 10 mM Tris-HCl, *p*H 8 0, by the addition of 0 3 ml saturated ammonium sulphate solution The solution was dialysed overnight against 1 1 10 mM Tris-HCl, *p*H 8 0 Polymerase enzyme incubations carried out with microsomes and cofactors as above Incubated enzyme used directly after high speed centrifugation to remove microsomes Polymerase assays carried out using nucleoplasmic enzyme Assay medium as for Mn^{2+} assay in Table 1, 15 μg DNA per assay *A*, Unincubated DNA, *B*, unincubated DNA + 50 μg aflatoxin B_1, *C*, DNA preincubated + 50 μg aflatoxin B_1, *D*, DNA preincubated + microsomes + cofactors without dimethylsulphoxide or aflatoxin B_1, *E*, DNA preincubated + microsomes + cofactors, *F*, DNA preincubated + microsomes + cofactors + aflatoxin B_1, *G*, nucleoplasmic enzyme preincubated + cofactors + dimethylsulphoxide, *H*, nucleoplasmic enzyme preincubated + microsomes + cofactors + aflatoxin B_1 Results are means of four assays on duplicate incubations ± s e *b*, Effect of microsomal metabolism of aflatoxin on the template capacity of a range of concentrations of DNA Assay conditions as in Fig 2*a* △, DNA preincubated + aflatoxin B_1 as in *C* in *a* ○, DNA preincubated with dimethylsulphoxide + microsomes + cofactors as in *E* in *a* ●, DNA preincubated + aflatoxin B_1 + microsomes + cofactors in *F* in *a* Results are means of triplicate assays ± s e administered *in vivo* on both the *in vivo* synthesis of RNA[11] and the activity of the RNA polymerases assayed in isolated nuclei *in vitro*[12]

We have examined the possibility that another metabolite of aflatoxin B_1 produced by microsomal systems might be involved in the inhibition of rat liver RNA synthesis by allowing the metabolism to proceed in the presence of DNA Figure 3*a* shows that a decreased template capacity resulted from incubating the DNA with microsomes+NADPH generating system alone The reason for this is not known, but it seemed to be dependent on microsomal metabolism as it was virtually eliminated if the cofactors were omitted from the incubations In spite of the decreased template capacity due to microsomes+cofactors alone, a further inhibition of the template capacity was apparent when microsomal metabolism of aflatoxin B_1 had proceeded in the presence of the DNA No comparable effect was observed when the aflatoxin B_1 was replaced by the dimethylsulphoxide vehicle alone To observe the effect, it was found necessary to have the DNA present during metabolism If aflatoxin B_1 was metabolized in the absence of DNA, and the DNA then added to the supernatant after spinning down the microsomes, no effect on the template capacity was observed Experiments in which the nucleoplasmic polymerase enzyme was incubated with aflatoxin B_1 and microsomes did not indicate that a reduced enzyme activity resulted This is in contrast to the recent finding of Moulé and Frayssinet[13], who reported that an unidentified microsomal metabolite of aflatoxin B_1 can inhibit the activity of bacterial RNA polymerase *in vitro* The reason for this difference is at present unknown and is being investigated

The inhibitory action of aflatoxin B_1 *in vivo* on hepatic RNA synthesis is accompanied by a reduced template capacity of the chromatin Such a mechanism could provide a basis for the equal inhibition by aflatoxin B_1 administered *in vivo* for the Mg^{2+} and $Mn^{2+}-(NH_4)_2SO_4$ stimulated polymerase activities observed in intact isolated nuclei The inhibition seems to require the metabolism of aflatoxin B_1 to an unstable metabolite by microsomal drug metabolizing systems One explanation of the apparent inhibition of the nucleoplasmic enzyme is that the effect of aflatoxin on the template might result in a greater difficulty in releasing the nucleoplasmic enzyme from the chromatin

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Peptide Formation mediated by Cyanate

CHEMICAL reactions of the sort that might have produced peptides from amino acids on the primitive Earth can be catalysed by kaolinite[1], montmorillonite[2], hydroxyapatite[3-5] and condensed phosphates[6-8] Hydroxyapatite has been suggested as a source of condensed phosphates because it yields pyrophosphate when reacted with cyanate[9] For this reason, and because phosphates polymerize amino acids, we have investigated whether peptide formation can be enhanced by cyanate added to hydroxyapatite or orthophosphates After we reported our preliminary results (at the national meeting of the American Chemical Society in Washington DC in September 1971), Choughuley *et al*[10] confirmed that orthophosphates catalysed the condensation of amino acids to peptides

Hydroxyapatite was prepared and aged in solution as outlined by Perloff[11] and the crystal phase was identified by X-ray diffraction The surface area was 50 m^2 g^{-1} as measured by nitrogen adsorption using the Brunauer, Emmett and Teller technique (BET) Reagent grade chemicals were used for the other phosphate phases (Table 1)

Mixtures of hydroxyapatite and glycine, with and without cyanate, were prepared by combining 1 M solutions of the corresponding reagents The mixtures were shell frozen and lyophilized Equal aliquots were weighed, sealed in 'Pyrex' test tubes, and heated at 95° C for varying times Attempts to condense glycine using hydroxyapatite or orthophosphates in aqueous solutions at 95° C for 10 days with and without cyanate failed The aqueous reactions were prepared by combining 10 ml each of 1 M solutions of glycine, *p*H 6 1, KCNO, *p*H 9 2, hydroxyapatite, *p*H 5 3, and orthophosphate (*p*H ranged between 2 8 and 12 5, depending on the orthophosphate used) These solutions were used for the solid state reactions The same procedure was followed with mixtures of various orthophosphates and glycine, with and without cyanate The reaction products were dissolved in water and aliquots analysed for linear glycine peptides on an automatic amino acid analyser, using the methodology for neutral and acidic amino acids from protein hydrolysates[12]

The synthesis of diglycine was verified by isolating the material eluted at 140 min, desalting it on 'Dowex'-50 (H^+ form) and comparing the isolated sample with the acid (6 N HCl, 110° C, 22 h) and enzymatically (leucine-aminopeptidase[13]) hydrolysed aliquots The unhydrolysed sample gave a chromatographic peak that coincided with that of authentic diglycine and an equal aliquot of the acid-hydrolysed sample gave the theoretical yield of glycine to within 5% Enzyme hydrolysis of a third aliquot reduced the amount of diglycine with a concomitant release of glycine Analysis by gas chromatography[14] of the N-trifluoroacetyl methyl ester derivative of the diglycine in the unhydrolysed

Table 1 Condensation of Glycine to Diglycine and Triglycine with Orthophosphates

Orthophosphate	Diglycine yield (%) *A*	*B*
Na_2HPO_4	0	1 85
Na_3PO_4 $12H_2O$	5 (1 4)	0
NaH_2PO_4 H_2O	0 5	7 35 (2 85)
$NH_4H_2PO_4$	0	1 6 (1 0)
$(NH_4)_2HPO_4$	0	0
K_2HPO_4	10 5 (3 9)	0 2
$CaHPO_4$	0	0 14
$Ca(H_2PO_4)_2$ H_2O	7 0	1 9

* Composition *A*, orthophosphate (10^{-3} M), glycine (10^{-3} M), *B*, orthophosphate (10^{-3} M), glycine (10^{-3} M), KCNO (10^{-3} M) The reactions were carried out in hypohydrous conditions for 20 d at 95° C The percentage of triglycine formed is shown in parentheses

fraction further confirmed that diglycine had been synthesized in the reactions studied.

Diglycine yields obtained with hydroxyapatite and sodium dihydrogen orthophosphate as a function of time are shown in Figs 1 and 2 The results show that glycine can be condensed to diglycine with hydroxyapatite or sodium dihydrogen orthophosphate in the absence of cyanate However, dipeptide yields were enhanced two to three-fold in the presence of cyanate

Because cyanate enhanced diglycine formation, we examined its action in combination with the orthophosphates shown in Table 1 The results show that, with the exception of NaH_2PO_4, the condensing action of cyanate with Na_2HPO_4, K_2HPO_4, and $CaHPO_4$ was, at best, marginal and actually suppressed the yields of diglycine with Na_3PO_4, K_2HPO_4 and $Ca(H_2PO_4)_2\ H_2O$

The partial transformation of orthophosphate to pyrophosphate at 126° C under anhydrous conditions[15] suggested that the polymerization of glycine at 95° C was related to polyphosphate formation To test this hypothesis, ^{32}P-labelled $NaH_2PO_4\ H_2O$ was added to 200 µl of 0 1 M NaH_2PO_4 and 100 µl of 0 1 M KCNO was added to half of this solution Both solutions were lyophilized, sealed and heated for 6 d at 95° C Each sample was dissolved in water and aliquots chromotographed on cellulose sheets using the solvent of Fuchs and Czeck[16] Spots located by autoradiography were excised and radioactivity was measured in a liquid scintillation counter

NaH_2PO_4 gave 2% pyrophosphate and 24% when cyanate was added This yield may include carbamyl phosphate, resulting from the reaction of orthophosphate with cyanate[17], and not resolved from pyrophosphate with the solvents used These results suggested that the production of higher yields of diglycine with NaH_2PO_4+KCNO was catalysed by pyrophosphate or carbamyl phosphate This possibility was tested by reacting equimolar dry mixtures of glycine with pyrophosphate and carbamyl phosphate for 6 and 10 d respectively at 95° C No diglycine (or larger peptides) was formed by pyrophosphate or carbamyl phosphate

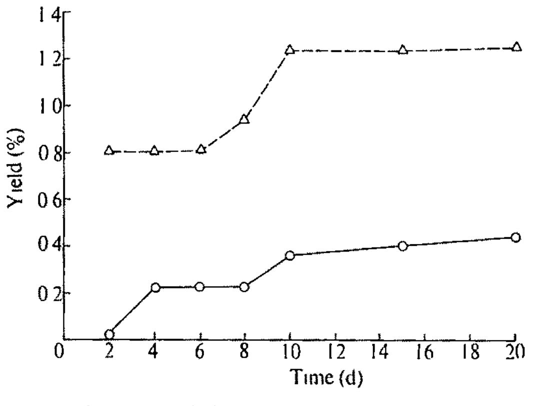

Fig. 1 Condensation of glycine to diglycine with apatite at 95° C △, Equimolar mixture (0 25 mmol each) of glycine, apatite and potassium cyanate ○, Equimolar mixture (0 25 mmol each) of glycine and apatite

The possibility that tripolyphosphate participated in the dimerization of glycine was explored by heating the anhydrous orthophosphates alone at 95° C for 20 d and assaying the thin-layer chromatography None of the orthophosphates that effectively dimerized glycine condensed to tripolyphosphate or higher linear phosphates

We believe that the orthophosphates in the absence of cyanate directly phosphorylated the carboxyl group of glycine and the glycine phosphate intermediate readily condensed with glycine Analogous reactions involving acylphosphate intermediates have been reported[18–21] Open or cyclic N-phosphoglycine cannot be excluded as an intermediate Related reactions have been reported[22]

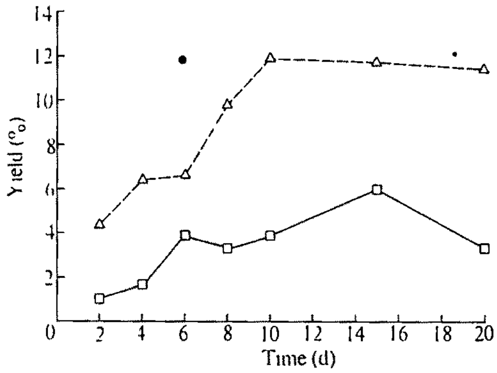

Fig 2 Condensation of glycine to diglycine and triglycine with orthophosphate at 95° C Percentage yield includes triglycine △, NaH_2PO_4 ($3\ 5\times10^{-3}$ M), glycine (10^{-3} M) and KCNO (2×10^{-3} M) ⊡, NaH_2PO_4 ($3\ 5\times10^{-3}$ M), glycine (10^{-3} M)

Our results show that when glycine is heated in the presence of apatite or orthophosphates, diglycine is formed The addition of inorganic cyanate increases the yields of diglycine but its action as a condensing agent extends only to some of the orthophosphates studied Even though glycine is effectively dimerized with $Na_3PO_4\ 12H_2O$, $NaH_2PO_4\ H_2O$, K_2HPO_4, and $Ca(H_2PO_4)_2\ H_2O$ there is reason to doubt the prebiotic significance of these reactions as these orthophosphates do not occur extensively in nature[23] We believe, however, that the reactions described here with hydroxyapatite and cyanate constitute a plausible model for condensation reactions on the primitive Earth, as apatite is the most thermodynamically stable solid calcium phosphate phase and is the form of phosphate most often found in nature Furthermore, cyanate could be reasonably considered a prebiotic compound as it is a derivative of urea which in turn is synthesized from methane, ammonia and water by electric discharges[24] or high energy electrons[25]

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Mechanical Instability of the Oxy-form of Sickle Haemoglobin

MUCH attention has been given to the molecular aspects of the deoxy form of sickle haemoglobin (Hb S) because sickling occurs with Hb S in the deoxygenated state The oxy form of Hb S, on the other hand, is believed to be similar to normal adult haemoglobin (Hb A) with respect to solubility[1,2], X-ray diffraction pattern[3], oxygen binding[4] and other properties During determination of oxygen equilibrium curves of Hb S, we noticed that a solution of oxyhaemoglobin S became turbid very easily when it was stirred or mixed The turbidity was found to be due to protein which was denatured by the mechanical force involved and/or by foaming Oxyhaemoglobin S denatured more quickly than oxyhaemoglobin A by mixing, stirring or sonication The rate of denaturation was dependent on the oxygen concentration in the medium, suggesting that an oxidative process was involved As demonstration of denaturation requires only a few drops of blood, water and shaking, this property can be used as a simple clinical test for the presence of Hb S

Haemoglobin solutions were prepared from heparinized blood[5] and used without further purification Haemoglobin solutions from normal (A), sickle cell disease (S) and sickle cell trait (AS) individuals were diluted into 2 5 ml of buffer to make a final haem concentration of about 60 μM The solution in a test tube (150×16 mm) was then mixed with a Vortex mixer for various time intervals After mixing, the solutions containing Hb S or haemoglobin from AS cells became turbid The precipitates were removed by centrifugation at 6,000*g* for 5 min at 5° C The absorption spectra of the haemoglobin remaining in the supernatant solutions after mixing for various time intervals are shown in Fig 1 The results clearly show that oxyhaemoglobin S denatures at about a ten-fold faster rate than does oxyhaemoglobin A Methaemoglobin was not formed in this experiment, as indicated by the flatness of the curves near 630 nm Figure 2 compares the denaturation rates of haemoglobin from S and AS blood with that of Hb A The rate of denaturation was calculated from the absorption change at 578 nm or 523 nm The latter is the isosbestic point between oxy and methaemoglobin and was used when methaemoglobin was formed Except in solutions below *p*H 5 0, no significant amount of methaemoglobin was formed by the mixing process The initial denaturation rate of haemoglobin prepared from persons with sickle cell trait (AS) was approximately one-half of that prepared from patients with sickle cell disease (Hb S) After denaturation of approximately 50% of the total haemoglobin in the AS haemolysate the rate decreased to that of Hb A, suggesting that Hb S in the haemolysate denatured independently from Hb A This result was examined further by densitometric quantitation of the haemoglobin bands separated by electrophoresis of the supernatant solution on cellulose acetate at *p*H 8 6 Before mixing, the electrophoresis showed 40% Hb S and 60% Hb A After mixing for 10 min, the supernatant haemoglobin contained 10% Hb S and 90% Hb A

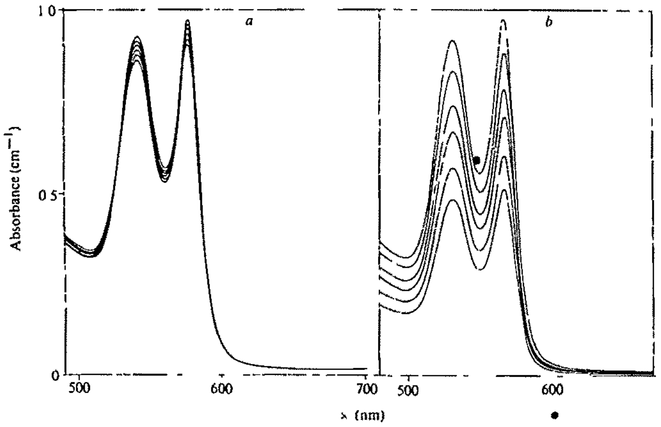

Fig 1 Absorption spectra of the haemoglobin in supernatant fractions after mechanical treatment Solutions of haemoglobin A (*a*) and S (*b*) in 0 1 M bis-Tris buffer, *p*H 7 0, were vigorously shaken by a Vortex mixer (Model K-500-4, medium position) for various time intervals (top to bottom 0, 2, 4, 6, 8, 10 min) The absorption spectra of the supernatants were measured with a Perkin-Elmer Coleman 124 Double Beam Spectrophotometer The top curve in each diagram is the spectrum of untreated haemoglobin and the rest are those corresponding to the treated samples

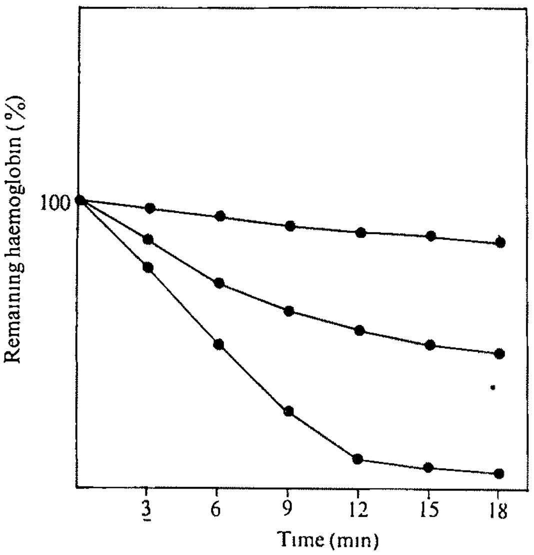

Fig 2 Rate of denaturation of haemoglobin prepared from normal (A) (upper curve), heterozygous (AS) (middle curve) and homozygous blood (S) (lower curve) Haemoglobin solutions were shaken mechanically for different time intervals at 23° C The haemoglobin in the supernatant was measured spectrophotometrically 0 1 M Tris-HCl buffer, *p*H 8

The effect of *p*H on the rate of denaturation of Hb S is shown in Fig 3 The denaturation rate was maximum at *p*H 8 5 Additional experiments demonstrated that the denaturation was also accelerated by increasing the ionic strength of the medium Sixty per cent denaturation of Hb S occurred, however, after shaking for 10 min haemolysates prepared and diluted in water, indicating that salts were not essential Denaturation was strongly temperature dependent, with Hb S being denatured more quickly at higher temperatures during mixing (Fig 4) Haemolysates prepared from a patient with homozygous Hb C disease and from newborn infants (Hb A+Hb F) were as stable as those prepared from normal adults (Hb A)

Although the exact mechanism of the denaturation of

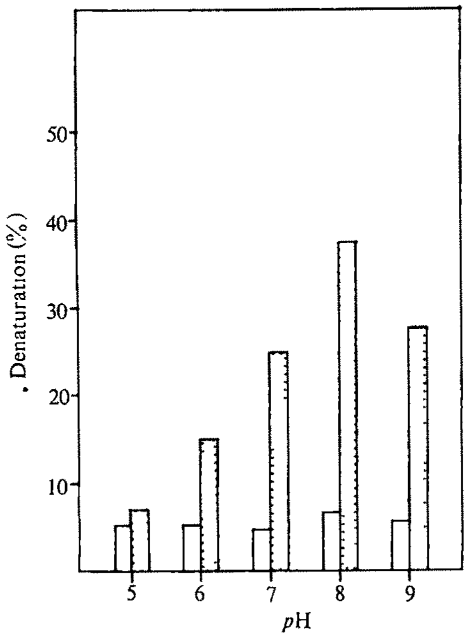

Fig. 3 Effect of pH on the mechanical instability of haemoglobin A (blank columns) and S (stippled columns) Denaturation (%) after 5 min shaking was compared at various pHs 0 1 M PO_4^{2-} buffer

Hb S is not known, the denaturation appears to involve an oxidative process, as the rate of precipitation of the fully oxygenated form was dependent on oxygen concentration It was also found that the deoxy form of sickle cell haemoglobin is more stable than the oxy form This difference in stability may be due to the inherent salt bridges present in the deoxy tetramer[6], but it could also be related to a lack of oxygen

As crystals of Hb A and Hb S have identical diffraction patterns[3], the gross structures of the molecules are considered to be similar The amino acid substitution at the sixth position of the β chain is external and therefore cannot be directly involved in the stability of the tetramer This non-polar substitution may, however, shift a dynamic equilibrium between the folded and the unfolded forms of the monomer (or dimer) in favour of the unfolded form because of the interaction between non-polar side chains (M F Perutz, personal communication)

Although deoxygenation produces sickling of erythrocytes containing Hb S, denaturation of oxyhaemoglobin S may also cause increased red cell rigidity and change red cell shape The presence of fully developed Heinz bodies (intracellular particles of precipitated haemoglobin) in untreated red cells from patients with sickle cell disease has been noted These inclusions may be related to the denaturation process described here Further examination of the mechanism of denaturation and the relationship of this denaturation to the properties of oxyhaemoglobulin S in intact red cells is currently in progress in our laboratories

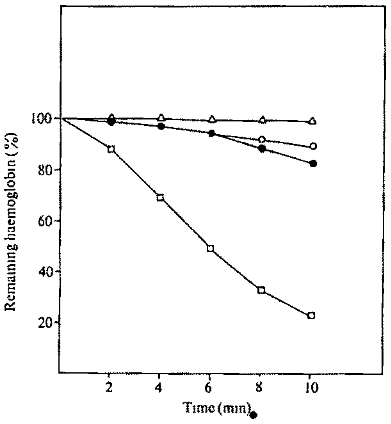

Fig 4 Effect of temperature on the rate of denaturation of haemoglobin A and S △, Hb A, 4° C, ○, Hb A, 25° C, ●, Hb S, 4° C, □, Hb S, 25° C 0 1 M Tris-HCl buffer, pH 8 0

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The Regulation of Vitamin D Metabolism

Vitamin D is hydroxylated in the liver to 25-hydroxycholecalciferol (25-HCC)[1], and this relatively inactive metabolite is further hydroxylated in the kidney to 1,25-dihydroxycholecalciferol (1,25-DHCC)[2] (Fig 1), the most active form, or to 24,25-dihydroxycholecalciferol (24,25-DHCC)[3], a less active metabolite The proportion formed of these metabolites is markedly influenced by diet[4,5], but there is dispute about how this is achieved One theory is that this involves parathyroid hormone and that this is the essential trophic factor which regulates the production of 1,25-DHCC[6] There is strong evidence against this view[7], however, and recent studies have cast further doubt thyroparathyroidectomized rats can increase production of 1,25-DHCC under appropriate dietary stimulus[8]

Fraser and Kodicek[9], however, in apparent support of this role of parathyroid hormone, recently showed convincingly that removal of the parathyroid and ultimobranchial glands in chicks almost abolished the production of 1,25-DHCC We have fully confirmed these results but show here that they were due to potentiation of an effect of vitamin D given to ensure post-operative survival In different conditions removal of parathyroid and ultimobranchial glands from chicks has little or no influence on vitamin D metabolism

When the parathyroid and ultimobranchial glands are removed from D-deficient chicks many of the birds die rapidly A higher survival rate can be achieved if a large dose of vitamin D_3 is given 24 h before operation, the procedure adopted by Fraser and Kodicek[9] Alternatives are either to ensure adequate intake of calcium post-operatively or to use less severely D-deficient chicks

We have studied chicks in all three conditions In our first experiment the parathyroid and ultimobranchial glands were removed from thirty chicks which had been fed a D-deficient

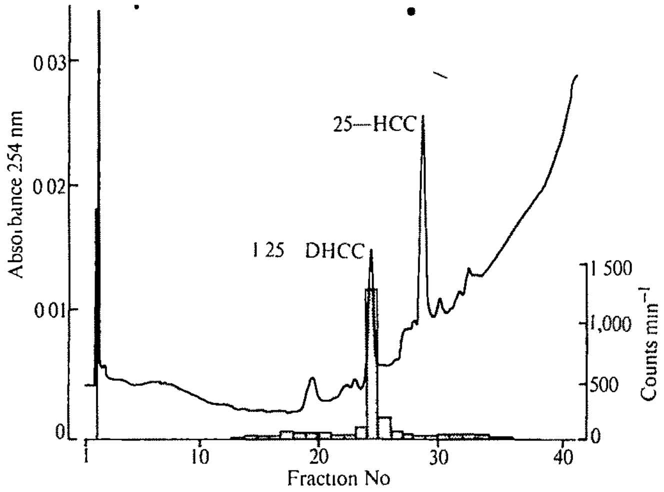

Fig. 1. The identification as 1,25-DHCC of a radioactivity peak from 'Sephadex' LH20 chromatography of a chick kidney homogenates. 75 ng synthetic 1,25-DHCC and 100 ng 25-HCC were added to a portion of the sample which was dissolved in methanol and injected into a 500 × 2.1 mm column (flow rate 1 ml min^{-1}, pressure drop 700 pounds per square inch) of ODS 'Permaphase' at 40° C on a Du Pont model 830 high-speed liquid chromatograph. Elution was performed with a linear gradient from water to methanol in which the methanol concentration increased by 5% (v/v) min^{-1}. The effluent was monitored at 254 nm and 30 s fractions were collected in a Gilson Microcol 80. The radioactivity in each sample was determined by liquid-scintillation counting and is shown as (stippled) columns against the ultraviolet trace after correction for dead volume. The radioactivity coincides exactly with the peak from added synthetic 1,25-DHCC.

diet for 3 weeks before operation (calcium 0.34%, phosphorus 0.54%). The chicks were allowed fat-free milk powder *ad libitum* post-operatively. Fourteen of the thirty survived and the remainder died in tetany. All fourteen sham-operated chicks survived operation. Table 1 shows that there was no change in the renal 1-hydroxylase activity for 20 h after operation.

These results seemed to be in direct conflict with those of Fraser and Kodicek and so a further series of experiments was carried out. Various D-deficient diets were used and in some experiments vitamin D was administered. In the others a reasonable survival rate was ensured by giving dried milk powder after operation or by calcium supplementation of the drinking water. Results are shown in Fig. 2. It is quite obvious that only the animals given vitamin D showed an effect of the operation, but as the groups were not all strictly comparable a confirmatory study was necessary. In this case we used chicks fed a D-deficient diet for 10 d only.

Table 1 Effect of Parathyroidectomy and Ultimobranchialectomy on 25-HCC-1-Hydroxylase Activity

Time after operation (h)	No. of birds	25-HCC-1-hydroxylase activity	Plasma (Ca) meq l^{-1}
0 (sham)	14	49±4.88	5.0±0.09
1	1	46	3.2
3	3	38±4.9	3.0±0.12
6	2	23±0.5	3.7±0.65
9	2	42±6.5	2.8±0.20
20	6	42±7.1	2.6±0.18

Chicks were anaesthetized with ether and maintained under positive pressure ventilation with an endotracheal tube. The kidneys were removed and a 4% (w/v) homogenate prepared in Tris-acetate buffer at 4° C. The assay was completed[10] using 25-HCC [26-(27)-*methyl*-^{3}H]-25-hydroxycholecalciferol (13.1 Ci mmol^{-1}) from the Radiochemical Centre, Amersham. Metabolites were separated on 'Sephadex' LH20 (ref. 5).

The enzyme activity is expressed as the mean ^{3}H % ± s.e. as 1,25-DHCC in kidney homogenates. Four replicate estimates were made from each bird. The plasma calcium is the mean ± s.e. of samples taken immediately before the birds were killed.

The results are unequivocal (Table 2, Fig. 3): vitamin D alone has a striking effect in depressing or abolishing 1-hydroxylase activity and in enhancing 24-hydroxylase activity, and removal of the parathyroid and ultimobranchial glands from chicks given vitamin D has a further marked effect in depressing 1-hydroxylase. The operation has no significant effect, however, in the absence of vitamin D. Clearly neither parathyroid hormone nor calcitonin is necessary for maintaining the enhanced 1-hydroxylase activity which is present in D-deficiency. Although Fraser and Kodicek[9] did not observe an effect of D alone, this may have been because they used rather fewer numbers and because they did not estimate 24,25-DHCC.

The most likely hypothesis which reconciles all the published data is that a major determinant of the type of metabolite produced is the intracellular calcium concentration within some critical compartment in the renal cells[5]. There is experimental support for this view. Calcium ions have a powerful inhibitory effect on the production of 1,25-DHCC *in vitro*[10,11]. Vitamin D is known to increase intracellular calcium[12] and this may be part of the explanation for its effect. Another factor may have been an increase in plasma phosphate, as this is also thought[13] to inhibit the activity of the enzyme.

Both these effects of vitamin D would have been potentiated by removal of the parathyroid and ultimobranchial glands. Absence of calcitonin may have enhanced the increase in intracellular calcium[14–16], and absence of parathyroid hor-

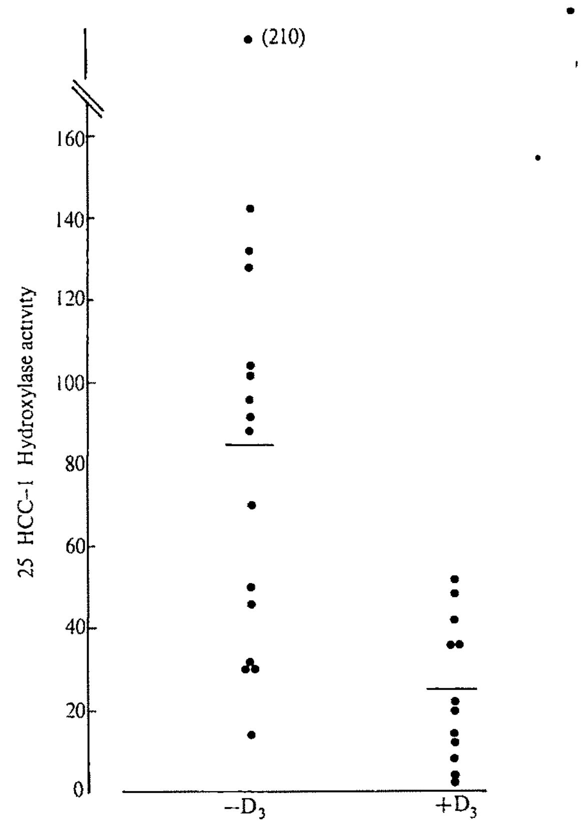

Fig. 2. 25-HCC-1-hydroxylase activity after parathyroidectomy and ultimobranchialectomy (PTUX). Each value is the mean of two to four replicate estimations from one bird 14 h after operation as a percentage of sham-operated controls. Four D-deficient diets were given. The Ca and P % contents were 0.34, 0.54, 0.68, 0.95, 1.0, 0.8, and 2.34, 0.54 respectively. Aluminium hydroxide (0.32%) was added to the 2.34% calcium diet to restrict phosphorus absorption. Results were similar in all diet groups. In one set of experiments cholecalciferol (2.5 μg) was given subcutaneously in ethanol 24 h before operation. The survival rates were sham 25/25, D$_3$+PTUX 12/19, PTUX only 16/27. Only the D$_3$ treated birds showed a significant fall in enzyme activity after PTUX. The plasma calcium immediately before death in the operated groups as a percentage of the sham controls was D$_3$+PTUX 68.4%±0.32, PTUX only 60.3%±0.42.

Table 2 Effect of Vitamin D$_3$ and of Parathyroidectomy and Ultimobranchialectomy (PTUX) on 25-HCC-1-Hydroxylase and 25-HCC-24-Hydroxylase Activity in Chick Kidney Homogenates

Operation	No of birds surviving	Treatment	25-HCC-1-Hydroxylase activity	25-HCC-24-Hydroxylase activity	Plasma (Ca) meq l^{-1}	Plasma (PO$_4$) mg per 100 ml
Sham	4/4	−Ca −D$_3$	14 39±0 75	0 33±0 08	4 6±0 19	4 8±0 11
	4/4	−Ca +D$_3$	3 90±0 85	5 11±0 81	4 9±0 19	7 2±0 60
PTUX	4/4	−Ca +D$_3$	0 41±0 14	10 37±0 66	3 1±0 43	12 7±2 60
	2/4	−Ca −D$_3$	11 81±1 78	0 40±0 10	3 5±0 45	6 6±0 10
Sham	3/4	+Ca −D$_3$	9 31±1 20	0 22±0 09	5 2±0 32	4 7±0 18
	4/4	+Ca +D$_3$	0 95±0 25	8 07±0 87	5 3±0 09	7 7±0 84
PTUX	4/4	+Ca +D$_3$	0 41±0 13	10 68±0 81	3 8±0 42	6 2±0 19
	4/4	+Ca −D$_3$	7 68±1 5	0 33±0 13	4 0±0 11	5 6±0 38

Thirty-two chicks maintained for 10 d on a D-deficient diet (0 34% Ca, 0 54% P) were divided into two equal groups one group (+D$_3$) received 2 5 μg cholecalciferol in 0 05 ml ethanol subcutaneously, the other (−D$_3$) received ethanol alone After 24 h the groups were further subdivided into sham or operated (PTUX) subgroups of eight birds After operation four of each subgroup (+Ca) were given 10 mg Ca h^{-1} in 15% glucose and four (−Ca) water only 14 h after operation blood was withdrawn by cardiac puncture for estimation of plasma calcium and inorganic phosphorus The birds were then killed by decapitation and two or three replicate kidney homogenates prepared for enzyme assay The enzyme activities are expressed as ng metabolite ±s e per 15 min produced from a homogenate of one quarter of a kidney Vitamin D$_3$ has a significant effect ($P<0\ 01$) in decreasing 1-hydroxylase and enhancing 24-hydroxylase activity PTUX has no effect ($P<0\ 05$) in the −D$_3$ group but has a marked effect ($P<0\ 01$) in the +D$_3$ group

mone certainly increased the plasma phosphate to extreme levels in one group (Table 2)

It is important to emphasize that our results are not in conflict with suggestions that parathyroid hormone may increase the production of 1,25-DHCC in some circumstances[9] But our experiments do show conclusively that parathyroid hormone is not an essential trophic hormone for the production of 1,25-DHCC Sadly, this seems to be another "beautiful and virtuous hypothesis butchered by a gang of ugly facts"[17]

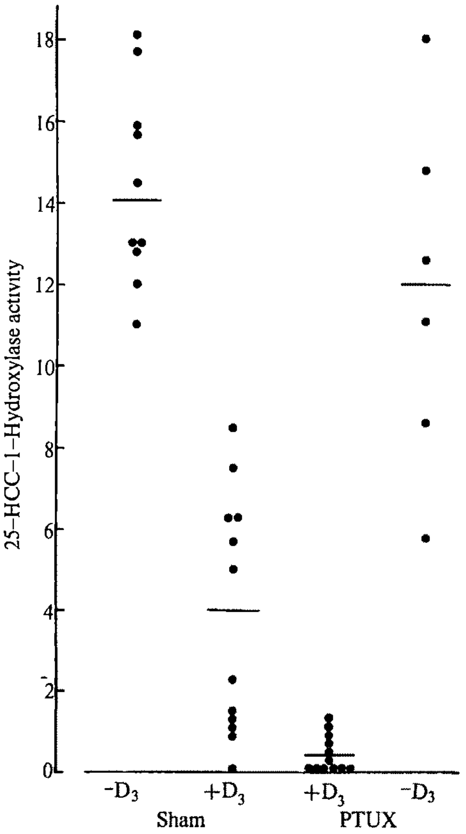

Fig. 3 The effect of cholecalciferol on 25-HCC-1-hydroxylase activity Parathyroidectomy and ultimobranchialectomy (PTUX) or sham-operation was carried out 24 h after subcutaneous injection of 2 5 μg cholecalciferol in ethanol (+D$_3$) or ethanol alone (−D$_3$) The renal 25-HCC-1-hydroxylase activity was measured 14 h later without post-operative calcium supplementation (−Ca group, see Table 2) Vitamin D has a marked effect ($P<0\ 01$) in both sham and PTUX groups PTUX decreased enzyme activity only in the +D$_3$ group ($P<0\ 01$) Each point represents the enzyme activity from one replicate expressed as ng 1,25-DHCC per 15 min from an homogenate of one quarter of a kidney

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Tolerance of Sk-incompatible Skin Grafts

ALLOANTIGENS expressed on one cell type but not on another provide the basis for homograft reactions directed against particular tissues The Sk alloantigens of mice are expressed on epidermal cells but not on haemopoietic cells[1] Thus C57Bl/6 (B6) mice that have been lethally irradiated and restored with (B6×A)F_1 spleen and bone marrow cells [abbreviated to (B6×A)-to-B6 chimaeras] invariably reject (B6×A) and A strain skin although they are permanent haemopoietic chimaeras Rejection is accompanied by the production of antibody which is cytotoxic for A strain epidermal cells but not for A strain haemopoietic cells of any type[2] The antigen thus recognized, Sk 1, is absent from all tissues of B6 mice, B6 epidermal cells carry the alternative alloantigen Sk 2

Table 1 Prompt Rejection of H-2-incompatible Skin Grafts by Radiation Chimaeras*

Recipients (lethally irradiated)	Haemopoietic cell donor	Skin graft From	Incompatible for	0	10	20	30	50	60	100	200	300	350
				Number of mice with surviving skin grafts									
17 B6 mice†	B6	SJL	H-2	17	17	1	0						
		A	H-2	17	17	1	0						
11 B6 mice†	(B6×A)	SJL	H-2	11	11	5	1	1	0				
		A	Sk only	11	11	11	11	11	11	7	2	1	0

(Columns 0–350: Days after skin grafting)

* 8×10^7 mixed spleen and bone marrow cells from B6 or (B6×A)F_1 donors were given intravenously within 24 h of lethal total body irradiation, as described previously[1] Donors and recipients were female mice about 3 months old

† Each mouse received A and SJL tail-skin grafts side-by-side on one graft bed within 24 h of irradiation

The ability of these chimaeras to reject A skin is ascribed to the fact that they lack Sk 1-bearing cells, assumed to be necessary for the maintenance of tolerance to Sk 1 antigen and so to A strain and (B6×A) skin grafts An indication that this is so was implicit in the original work on Sk antigens Thus rejection of donor skin grafts by chimaeras is considerably delayed if the grafts are made immediately after irradiation and haemopoietic restoration rather than some weeks later, suggesting that a skin graft provides sufficient Sk 1 antigen to maintain some degree of tolerance[1]

Table 2 Acceptance of Sk-incompatible (A) Skin Grafts by Lethally Irradiated B6 Mice restored with (B6×A) Haemopoietic Cells* and given Systemic Injections of Dispersed A Strain Epidermal Cells

Treatment of chimaeras	0	100	200	300	400	500
	Mice with surviving skin grafts/mice grafted					
None	37/37	17/37	2/37	0/37		
A strain epidermal cells‡	21/21	21/21	19/20	19/20	13/17	10/15

(Columns 0–500: Days after grafting of A strain skin†)

* See footnote to Table 1

† Skin was grafted within 24 h of irradiation

‡ Trypsinized viable dispersed tail epidermal cells[2], 2 7×10^6 given intravenously and 2 7×10^6 given intraperitoneally, within 24 h of irradiation, followed by 2 5×10^7 given intraperitoneally on day 72

Alternatively, the delay in rejection of early skin grafts could be attributed to immunosuppression caused by irradiation But this explanation is rendered unlikely by the results in Table 1, B6 lethally irradiated mice were restored with either B6 or (B6×A) haemopoietic cells, and each then received grafts of SJL and A skin All H-2-incompatible skin grafts were rejected within a period little, if any, longer than that of H-2-incompatible skin grafts on normal mice [Isolated Sk-incompatibility, represented by the A skin grafts on (B6×A)-to-B6 chimaeras (Table 1) gave rise to the usual somewhat protracted rejection of all grafts[1]] Thus maintenance of tolerance rather than immunosuppression is the likely cause of the chimaeras' delay in rejecting early skin grafts

The use of much larger A strain skin grafts on (B6×A)-to-B6 chimaeras, intended to supply more Sk 1 antigen and so increase the degree of tolerance, did not give decisive results So we next tried the effect of dispersed viable A strain epidermal cells[2] injected intravenously and intraperitoneally at the time of irradiation and restoration As Table 2 shows, this achieved a high degree of tolerance, of fifteen (B6×A)-to-B6 chimaeras receiving these systemic inoculations of A strain epidermal cells, ten retained their A strain skin grafts for the entire period of observation (>500 d)

It was then necessary to show that the effect of the epidermal cells was specific for Sk 1 The experiment was repeated including a control group of twenty-four chimaeras receiving B6 (host-type) epidermal cells (Table 3), these produced no delay in the rejection of A skin grafts On this occasion the degree of tolerance produced by A epidermal cells was not so marked (possibly because of a different schedule of inoculation) but six out of twenty-seven chimaeras of this group retained their A grafts throughout the observation period (>400 d)

As in the previous study[1], every chimaera rejecting donor skin was typed by haemagglutination and cytotoxicity tests for H-2, and none showed loss or decline of chimaerism, that is, their erythrocytes and lymph node cells gave H-2 reactions identical to the donor (B6×A)

Table 3 Sk 1 Specificity of the Tolerance produced by A Strain Epidermal Cells

Treatment of chimaeras*	0	100	200	300	400
	Mice with surviving skin grafts/mice grafted				
None	7/7	4/7	1/7	0/7	
B6 epidermal cells‡ (control)	24/24	9/24	2/24	0/24	
A strain epidermal cells‡	27/27	25/27	19/27	10/27	6/27

(Columns 0–400: Days after grafting of A strain skin†)

* Of (B6×A)-to-B6 constitution, see footnote to Table 1

† Skin was grafted with in 24 h of irradiation.

‡ Trypsinized viable dispersed tail epidermal cells, 1 5×10^6 given intravenously and 3 5×10^6 given intraperitoneally, within 24 h of irradiation, followed by 1×10^7 given intraperitoneally on day 50, and 6×10^6 given intraperitoneally on day 85

These results confirm our previous conclusions that these chimaeras reject donor skin because they are not immunologically tolerant to Sk 1 antigen, and that this is a result of the absence of Sk 1-bearing cells in the chimaeras. By supplying Sk 1 antigen, in the form of systemically inoculated epidermal cells, the rejection response to donor skin can be largely or entirely eliminated.

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Localization and Release of Glutamic Acid in Relation to the Hippocampal Mossy Fibre Pathway

ABUNDANT clinical and experimental evidence indicates that the hippocampus is involved in temporal lobe epilepsy[1,2]. Some of the symptoms of excitation associated with the disease may be related to the marked tendency of the hippocampus to produce seizures in response to mechanical, electrical and chemical stimuli[3]. Focal discharges in the temporal lobe could spread through direct afferents to the nearby entorhinal cortex[4]. Excitatory projections from entorhinal neurones form the final link in the chain between the sensory neocortex and the hippocampus by making synaptic contact with granule cells of the dentate gyrus. Axons arising from the granule cells synapse, in turn, on the apical dendrites of CA3-4 hippocampal pyramidal cells. These axons comprise the mossy fibre pathway[5].

Repetitive stimulation of afferent fibres terminating on pyramidal cell apical dendrites is often associated with "spike complications" which develop after discharges, then ictal spikes[3]. Accumulation of a depolarizing substance in the vicinity of receptors on the tightly packed CA3-4 dendrites could establish an excitable focus with a low threshold for afferent stimuli. Certain acidic amino acids depolarize brain neurones[6,7] and could, in some circumstances, alter the excitability of apical dendrites. Therefore, we determined the concentrations of free amino acids in the mossy fibre layer, and compared these concentrations with those in the apical dendrites of CA1 pyramidal cells which do not receive mossy fibres.

Whole brains were rapidly removed from cats asphyxiated with CO_2, frozen on the stage of a sliding microtome, and sectioned horizontally to expose the hippocampus. Tissue samples from the dendritic layers were dissected with the aid of a stereomicroscope and kept frozen until the amino acid concentrations were determined with an amino acid analyser. The most remarkable finding was the large concentration of free glutamine and glutamic acid in the mossy fibres of the CA3 area, relative to the concentrations in an analogous area of CA1 (Table 1). Five other amino acids (aspartate, threonine, serine, alanine, and glycine) were detected in the 5–12 mg samples, but were more uniformly distributed[8]. We also determined the relative enzymatic activity of L-glutamic acid dehydrogenase (EC 1.4.1.3) which catalyses the production of glutamic acid in cerebral tissue[9,10]. The activity of the enzyme in the mossy fibre layer was more than twice that in the CA1 apical dendrite layer. The presence of this zinc-metalloenzyme[11] in the mossy fibre pathway is noteworthy, as histochemical[12,13], autoradiographic[14,15], and ultrastructural studies[13] have indicated that high concentrations of zinc are localized in large preterminal boutons synapsing on CA3 apical dendrites. Alternatively, the proposal[16] that neurotransmitters may be stored as trace metal chelates may also be important in the mossy fibres, as glutamate forms ligand bonds with zinc[17].

Table 1 Comparison of CA1 and CA3 Apical Dendritic Layers of Hippocampal Pyramidal Cells

	CA1	CA3
Free amino acids *† (nmol mg^{-1} protein)		
Aspartic acid (4)	15.3 ±2.4	19.9 ±0.6
Glutamine (3)	26.5 ±2.3	41.5 ±4.5
Glutamic acid (4)	44.6 ±5.1	102.7 ±6.4
L-Glutamic acid dehydrogenase *‡ (units mg^{-1} protein, $n=3$)	2.79±0.34	6.54±0.28
Zinc-dithizonate§ (histochemical reaction)	+	+++
^{65}Zinc uptake *in vivo*‖ (autoradiography)	△	△△△
Mossy fibre boutons¶	Absent	Present

* Results are expressed as means ± s.e., numbers of cats in parentheses. Values for individual cats were obtained by averaging two or more analyses. Protein was measured by the Lowry method.

† Aspartic acid, glutamine and glutamic acid were assayed from tissue samples with a Beckman 120C amino acid analyser after extracting into 5% trichloroacetic acid, centrifuging at 23,500*g* for 30 min, lyophilizing the supernatant, and resuspending the residue in lithium-citrate buffer (*p*H 2.8). Aspartic values are not significantly different ($P>0.05$). Glutamine and glutamic values are significantly different ($P<0.05$, $P<0.025$, respectively, two-tailed, two sample *t* test).

‡ A unit of enzyme activity represents 1 μmol of glutamic acid synthesized h^{-1}. Activity was measured kinetically by observing the rate of disappearance of NADH[9] at 340 nm. Values significantly different ($P<0.005$, two-tailed, two sample *t* test).

§ +, Faint colour, +++, intense colour (frozen sections after diphenylthiocarbazone, 100 mg kg^{-1}, intraperitoneal injection[12]).

‖ △, Few positron tracks, △△△, multiple positron tracks[15].

¶ By light and electron microscopic analyses[5].

The relatively high concentration of glutamic acid in the mossy fibre layer prompted an investigation to determine if glutamate could be released by activation of the mossy fibres. In cats anaesthetized with methoxyflurane the overlying neocortex was aspirated and a collecting cup, positioned on the hippocampal surface, was continuously superfused with Ringer-Locke solution. A bipolar electrode within the cup recorded the surface electrical activity. This was displayed on an oscilloscope throughout the course of the experiments. Mossy fibres were activated by lowering a bipolar stimulating electrode into the entorhinal cortex until single stimulus pulses evoked wave-forms characteristic of pyramidal cell excitation[5]. Entorhinal stimulation significantly increased the rate of glutamate release (Fig. 1). An area immediately adjacent to the cup was also stimulated electrically as a test for specificity. Local stimulation elicited only a modest change in the release of glutamic acid (Fig. 1).

The presence of large amounts of glutamate in a circumscribed area of the hippocampus and the release of this excitatory amino acid in response to mossy fibre activation suggest that endogenous glutamate could initiate or reinforce the production of hippocampal ictal spikes. The relationship which may exist in the hippocampus between neuronal activity and glutamic acid is evident from reports that sustained release of L-glutamic acid from micropipettes in close proximity to pyramidal cells induces either a fast synchronized rhythm or seizure discharge[18]. Furthermore, the rate of glutamate release from experimental cortical foci increases dramatically during seizure activity[19]. Aberrations in glutamic acid meta-

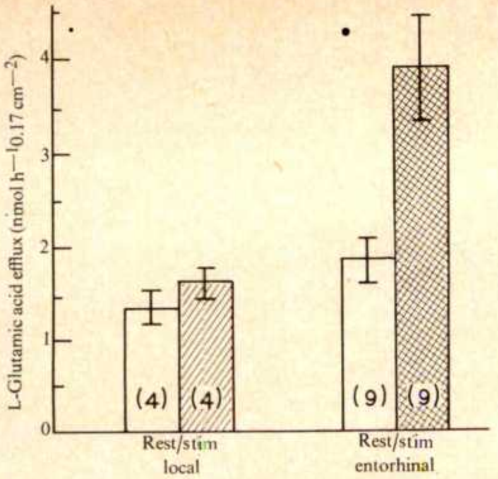

Fig. 1 Release of glutamic acid from cat hippocampus in the absence of stimulation (resting state) and in response to local and entorhinal electrical stimuli. Glutamate concentrations (nmol) in superfusates (cup area, 0.17 cm^2; volume, 0.25 ml; Ringer-Locke solution, 13.6 μl min^{-1}) were determined by a micro-enzymatic method[23]. Stimulus pulses (3 Hz, 0.5 ms duration, 10–40 V, for 1 h) were delivered to the entorhinal cortex or the hippocampal surface through bipolar electrodes (28 gauge stainless steel wire, 1.2 kΩ resistance, insulated except for the tips, <1 mm tip separation). The bars represent means (± s.e.m.), number of animals in parentheses. Entorhinal stimulation significantly increased glutamate efflux when compared with release during rest ($P<0.025$, paired t test) and during local stimulation ($P<0.05$, two sample t test).

bolism in the brains of epileptics and of animal models of epilepsy are well known and a subject of current interest[1,2,20–22]. Our results, linking glutamic acid with the mossy fibre pathway, should aid in the understanding of the interrelationships between cytological, physiological, and biochemical factors which may participate in the genesis of hippocampal seizures.

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Pattern of Remyelination in the CNS

For more than a decade it has been known[1–3] that glial cells are capable of forming new myelin sheaths around demyelinated axons in the central nervous system (CNS) but it is not known whether the new myelin is formed into segments bounded by true nodes and, if it is, whether the internodal length is appropriate to the axon diameter or inappropriately short as in remyelinated peripheral fibres. The different relationship between the myelin forming cell and axon in central and peripheral fibres makes this difficult to predict. Each Schwann cell in the peripheral nervous system (PNS) forms a single internode, whereas in the CNS a single oligodendrocyte usually forms a cluster of internodes on adjacent fibres[4,5]. We have therefore studied the pattern of remyelination during recovery from acute experimental compression of the spinal cord, a lesion in which myelin destruction with preservation of axon continuity (demyelination) is followed by remyelination which commences in the third week[6].

Observations were made on lesions from three adult cats and the findings compared with eight normal controls. In the experimental animals, a laminectomy was performed at L.1 under pentobarbitone anaesthesia and the exposed posterior columns compressed through the intact dura for up to 3 h. Further details of the method of compression are given elsewhere[6]. The animals were killed under anaesthesia 21 d, 1 month and 3 months after compression, by retrograde perfusion through the abdominal aorta with 4 or 5% glutaraldehyde in phosphate buffer at pH 7.4 followed by Dalton's fluid[7]. The compressed segment of the cord was removed. Part of it was cut into thick (60 μm) sections on a freezing microtome and teased under a dissecting microscope[8]. Measurements of diameter and internodal length of individual fibres were made using the method described by McDonald and Ohlrich[8]. The remainder was prepared for conventional light and electron microscopy.

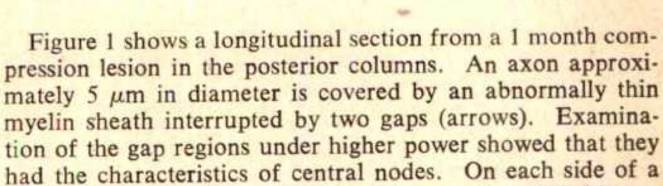

Fig. 1 One-month lesion. An axon approximately 5 μm in diameter is covered by an inappropriately thin myelin sheath. The arrows mark nodes (see text). The internodal distance is 67 μm. Bar = 10 μm.

Figure 1 shows a longitudinal section from a 1 month compression lesion in the posterior columns. An axon approximately 5 μm in diameter is covered by an abnormally thin myelin sheath interrupted by two gaps (arrows). Examination of the gap regions under higher power showed that they had the characteristics of central nodes. On each side of a gap, the myelin lamellae terminated in cytoplasm-filled loops. Most of these were attached to the axolemma by transverse bands, the spacing between which was less regular than in normal animals. Some of the loops, although adjacent to the axolemma, were not attached to it. The internodal segment in Fig. 1 is 67 μm long and was one of a series of four consecutive internodes ranging from 67 to 85 μm in length. The myelin was uniformly thin in each. The minimum internodal length found in normal fibres of this diameter is 300 μm[8]

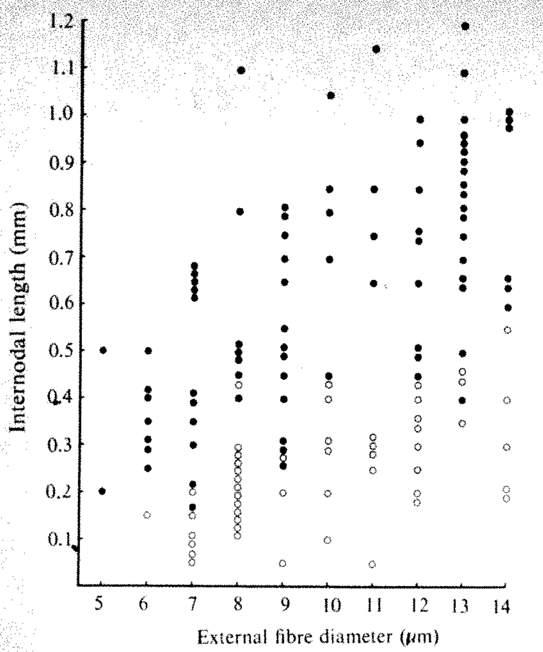

Fig. 2 Relationship between internodal length and external fibre diameter. (●), Fibres from normal animals; (○), fibres from compression lesions. (Details in text.)

(cf. Fig. 2). Although short internodes occur in the grey matter of the normal rat brain[9], they are not found within the posterior columns of the cat spinal cord[8]. We conclude that these abnormally thin and short segments of myelin bounded by a node at each end are remyelinated internodes.

Further quantitative information about the dimensions of the remyelinated segments was obtained from light microscopic study of single fibres isolated by teasing from the peripheral parts of the lesion. Many fibres had short segments of thin myelin separated by nodal gaps from myelin of normal thickness. Measurements were made of fifty such fibres, and the internodal length of the thin segments compared with the internodal length of fibres of comparable diameter teased from three normal animals (Fig. 2). The diameter assigned to the fibre containing the thin segment was the mean of the diameters of the adjacent segments of the same fibre with myelin of normal thickness. As previously reported[8], there was a direct relationship between internodal length and fibre diameter in the normal central fibres. Figure 2 shows that the majority of the thin segments have internodal lengths which are approximately 50% shorter than those found in control fibres of the same diameter. We conclude that during the first 3 months at least, newly formed internodes are inappropriately short for the fibre diameter. We are currently investigating acute compression lesions of longer duration to determine the extent to which the appropriate internodal length and myelin thickness are restored.

Other experiments have shown that Schwann cells of peripheral origin are capable of migrating into the spinal cord and forming myelin around central axons[10,11]. The question therefore arises as to whether the short internodes in the present study were formed by glial or by Schwann cells. Two sets of observations show that the remyelination reported here was effected by glial cells. First, many of the remyelinated single fibres were isolated from animals in which careful light and electron microscopic examination of the remainder of the lesion failed to show Schwann cells. Second, on the rare occasions in one animal when remyelination by Schwann cells did occur, it was distinguished by a thick layer of cytoplasm in the paranodal region and a basement lamina which enclosed the whole internode. The thick cytoplasmic collar and basement lamina are absent from myelin sheaths of glial origin. The structure of the myelin forming processes resembles that of the oligodendrocyte, and was readily distinguished from that of the fibril-containing astrocytes and the phagocytes[6]. We conclude that the thin internodes are formed by oligodendrocytes.

The extent to which remyelination occurs in the human CNS is still uncertain[11]. Our demonstration of inappropriately short internodes may provide a new criterion for its identification. However, before interpreting the scanty direct[12] and indirect[13] evidence for short internodes in multiple sclerosis as signs of remyelination, it is essential to have more information about the normal variation in length of internodes in different parts of the CNS in man, as in some species very short internodes are a feature of normal nerve fibres in the grey matter[9].

Some recovery of function is characteristic of demyelinating lesions in the CNS. This raises the question of whether remyelination might restore transmission in fibres with conduction block due to demyelination[14]. Our study shows that the known morphological prerequisites for saltatory conduction are present in the remyelinated fibres. An examination of the physiological properties of the remyelinated fibres, and determination of the factors which govern the occurrence and completeness of remyelination in different types of central lesion, remain to be carried out.

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Human x Mouse Somatic Cell Hybrid Clone secreting Immunoglobulins of both Parental Types

HYBRIDS between two distinct differentiated cell types usually do not express the differentiated characteristics of either parental cell. The synthesis of enzymes necessary for the metabolism of the cell continues, while the synthesis of specialized products of differentiation often is suppressed[1]. Mouse myeloma cells, after fusion with mouse fibroblasts, follow this pattern; that is, the hybrid cells cease synthesis of immunoglobulin[2,3]. A myeloma × lymphoma hybrid, however, continues secretion of immunoglobulin[4,5]. We report

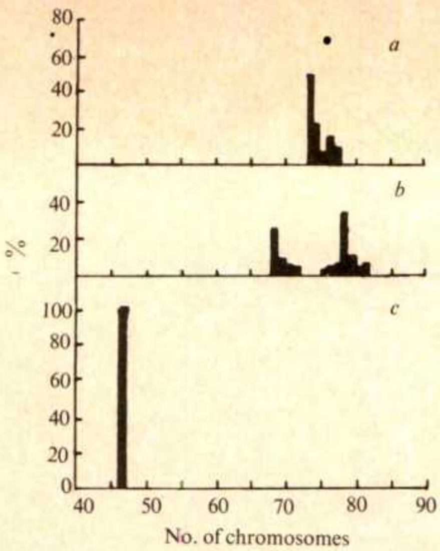

Fig. 1 Normal histogram showing the distribution of chromosomes from (*c*) human peripheral blood lymphocytes, (*b*) TEPC-15 mouse myeloma cells, and (*a*) clone H1C11 hybrid cells.

here the isolation of a hybrid clone, resulting from fusion of mouse myeloma cells secreting immunoglobulin of known specificity and human peripheral blood lymphocytes not secreting detectable immunoglobulin. The hybrid cells continue secretion of mouse immunoglobulin and initiate synthesis and secretion of human immunoglobulin.

TEPC-15 myeloma cells from Balb/c strain mice grow slowly *in vitro* in Eagle's minimum essential medium supplemented with 20% foetal calf serum and 150 mM L-glutamine (complete MEM). The cells remain viable in culture for 4–6 weeks, adhering to the bottom of plastic flasks. They continue synthesizing mouse IgA with antibody activity for *Pneumococcus* C polysaccharide[6]. Normal human peripheral blood lymphocytes remain viable *in vitro* for 4–5 d, after which rapid disintegration of the cells occurs spontaneously.

TEPC-15 myeloma cells and normal human peripheral blood lymphocytes were fused with the aid of inactivated Sendai virus. Two-week-old "cultures" of TEPC-15 cells were used as one parent. One thousand to five thousand TEPC-15 cells were incubated in a 30 ml Falcon flask at 4° C with 400 haemagglutinating units of β-propriolactone-inactivated Sendai virus (grown and inactivated according to the methods described by Klebe *et al.*[7]. After the virus was added, 2×10^6 purified human lymphocytes were added to the cultures. The lymphocytes were obtained by sterile venipuncture from a healthy donor (J. S.), separated from erythrocytes by gravity sedimentation for 3–4 h, followed by incubation for 1 h in a plastic Petri dish, to eliminate the adherent granulocytes. The lymphocyte parental population was 99% pure by morphological criteria. The cultures were incubated at 4° C for 20 min. They were then incubated at 37° C for another 30 min, after which warm complete MEM was added. The cultures were placed in an incubator at 37° C and gassed continuously with 5% CO_2 and 95% air. The medium was decanted completely every 4–5 d thereafter. All human parent cells disappeared from the cultures within 2 weeks. Many large cells could be seen at this time. Six to eight weeks after fusion, when discrete colonies could be seen, the cells were replated. After a further 4 weeks, clones were isolated. Three months after fusion (4 weeks after isolation) clone H1C11 grew in both mixed monolayer and suspension culture, and doubled every 35 h.

Metaphase chromosome spreads were prepared from this clone approximately 5 weeks after isolation. Vinblastine was used to arrest the cells in metaphase (0.075 M KCl hypotonic solution); fixation was in 1:3 acetic acid: methanol, and the preparation was air dried on microscope slides[8,9]. Analysis of human parental cell chromosomes prepared by this method showed a normal human chromosome constitution of 46 XY. TEPC-15 cells had a bimodal distribution of chromosomes, with clustering at sixty-eight and seventy-eight telocentric chromosomes (Fig. 1). The spreads with seventy-eight chromosomes had one very long telocentric chromosome with a secondary constriction (Fig. 2*a*). The human chromosomes, with the exception of the D and G groups, were distinguished readily from all the TEPC-15 chromosomes. Metaphase spreads from clone H1C11 revealed a modal number of seventy-three chromosomes (Figs 1 and 2), including two marker metacentric chromosomes characteristic of the human C and E groups (Fig. 2*b*). The very long myeloma marker telocentric chromosome was not present in any of the hybrid metaphase spreads examined. Eighty per cent of the spreads contained these two human metacentric markers, another 16% contained one and in only 4% of the chromosome spreads could no human marker chromosome be found.

The hybrid cell line continued producing myeloma protein with antibody activity as detected by agar gel diffusion. Precipitin lines formed in 1.0% agar between wells containing culture medium concentrated ten-fold and specific antiserum prepared in rabbits against mouse Ig, in which myeloma

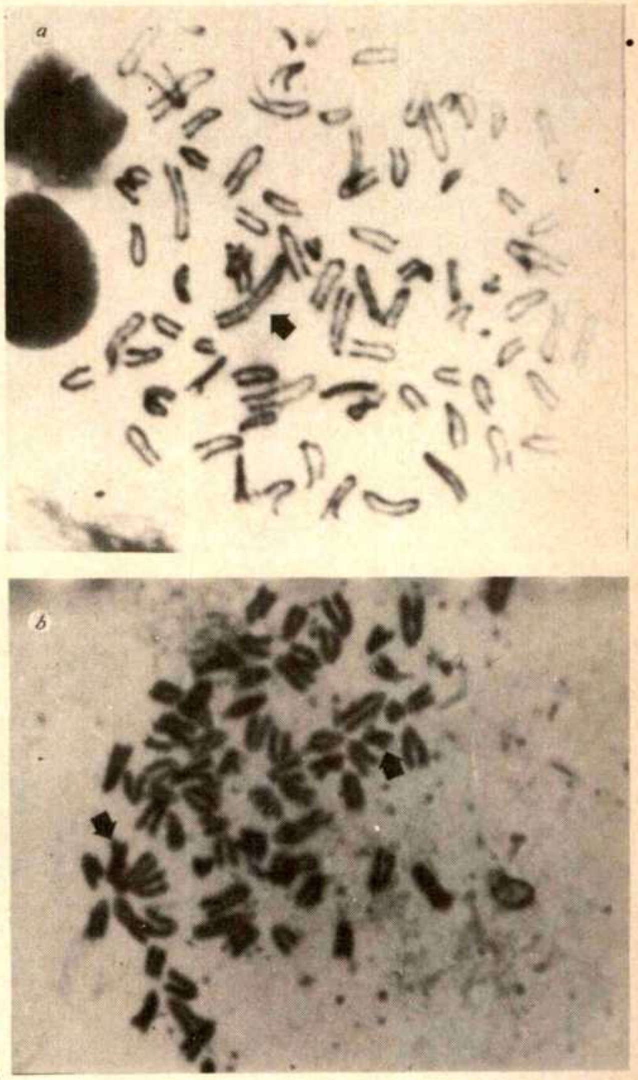

Fig. 2 *a*, Metaphase chromosome spread of a TEPC-15 mouse myeloma with eighty chromosomes. Note the very long telocentric marker. *b*, Metaphase chromosome spread of a clone H1C11 hybrid cell. Note the two human marker metacentric chromosomes (arrows) (×550).

protein served as an antigen. Precipitin lines also formed between wells containing ten-fold concentrated medium from the hybrid culture and *Pneumococcus C* polysaccharide, indicating that the Ig secreted by the hybrid retained its antibody activity.

To examine the hybrid cell cultures for the synthesis and secretion of human and mouse Igs, culture medium supernatant from hybrid cells incubated for 16 h with 30 μCi ^{3}H-leucine was precipitated directly with either rabbit antiserum to mouse Ig or rabbit antiserum to human Ig, and electrophoresed on SDS-containing acrylamide gels[10]. Immunoprecipitates formed after the hybrid cell culture supernatant was incubated with antimouse Ig contained optical density and radioactivity peaks co-migrating with heavy chain dimer (H_2) and light chain dimer (L_2), and an optical density peak co-migrating with precipitating γ globulin (H_2L_2) (Fig. 3). Hybrid cell culture medium precipitated with rabbit anti-human Ig showed three distinct peaks co-migrating with H_2L_2, H_2 and L_2. There was a shoulder on the H_2L_2 peak which, in addition to the H_2 and L_2 peaks, is associated with peaks of radioactivity (Fig. 3).

To determine whether individual hybrid cells synthesized both human and mouse Igs, clone H1C11 was examined by the fluorescent antibody technique. Fixed hybrid cell preparations were stained with fluorescein-conjugated rabbit antiserum to human Ig. Fluorescent cells were identified and the fluorescence was then quenched with strong ultraviolet irradiation. The cells were then stained with fluorescein-conjugated rabbit antiserum to mouse Ig (Fig. 4). The results indicate that most, if not all, of the cells synthesized both human and mouse Ig. The same experiment, done in the reverse order, yielded essentially the same results. The pattern of staining with antiserum to both human and mouse Ig was similar to the pattern of staining found with large lymphocytes and plasma cells[11]. Staining with fluorescein-conjugated antiserum to mouse Ig could be blocked by previous addition of excess unconjugated antiserum to mouse Ig or with excess exogenous mouse Ig but not by antihuman Ig or exogenous human Ig. Staining with fluorescein-conjugated antiserum to human Ig could be blocked by antihuman Ig or human Ig but not by antimouse Ig or mouse Ig, showing the specificity of the staining.

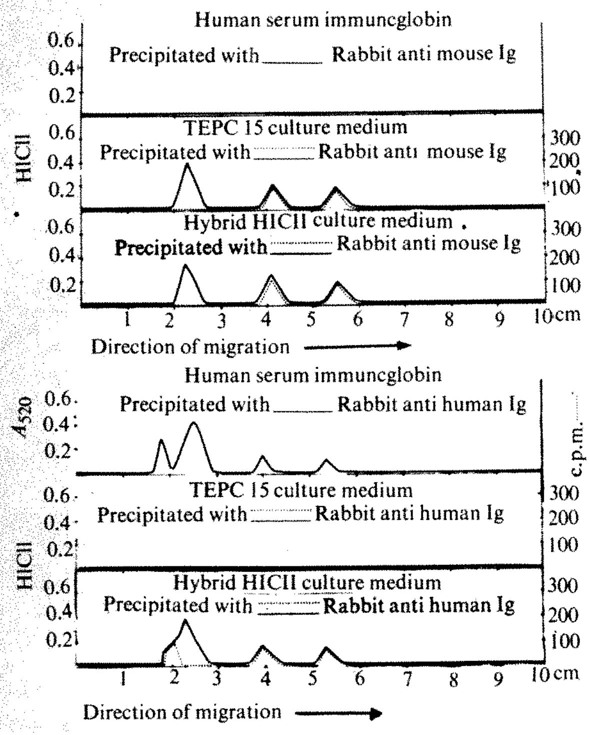

Fig. 3 Patterns of migration of human, mouse and hybrid clone H1C11 secreted Ig. Human serum was purified by $(NH_4)_2SO_4$ precipitation; the Ig was then directly precipitated with rabbit antiserum to human Ig. Hybrid cells and TEPC-15 C3 (culture-adapted myeloma cells) were incubated with 30 µCi ^{3}H-leucine in normal culture medium (excess cold leucine present) for 16 h. The cells were pelleted and the supernatant precipitated with rabbit antiserum to human Ig or rabbit antiserum to mouse Ig. The precipitates (human, mouse, hybrid) were redissolved in 0.1% SDS, and electrophoresed on 10 cm, SDS-containing, 5.0% acrylamide gels for 7 h (at 50 V). The gels were then stained with Coomassie blue, destained and scanned in a Gilford spectrophotometer with linear transport mechanism. The gels containing myeloma and hybrid medium were sliced (thirty slices per gel) and counted in a liquid scintillation counter. Bovine serum albumin added to hybrid culture medium and then precipitated with anti-BSA, yielded optical density bands corresponding to precipitating antibody (IgG) and BSA (68,000 molecular weight) but no radioactivity above background was detectable. Albumin (arrow 1) and haemoglobin (arrow 2) were used as markers for molecular size estimation.

Fluorescent antibody		
TEPC 15 (mouse myeloma)	H1C11 (hybrid)	Lymphocytes (human)
FITC anti mouse Ig >90%	FITC anti mouse Ig >90%	FITC anti mouse Ig 0%
↓ Quench	↓ Quench	↓ Quench
FITC anti human Ig 0%	FITC anti human Ig >90%	FITC anti human Ig 40–50%
FITC anti human Ig 0%	FITC anti human Ig >90%	FITC anti human Ig 40–50%
↓ Quench	↓ Quench	↓ Quench
FITC anti mouse Ig >90%	FITC anti mouse Ig >90%	FITC anti mouse Ig 0%

Figures represent percentage of cells staining with fluorescent antiserum.

Fig. 4 Design of fluorescent antibody experiments. Both antisera were prepared by immunization of rabbits, $(NH_4)_2SO_4$ precipitation, and conjugation with fluorescein isothiocyanate (FITC).

Clone H1C11 is a hybrid resulting from the fusion of one mouse myeloma cell with one human lymphocyte. Absence of the very long acrocentric marker mouse chromosome indicates that the myeloma cell parent contained sixty-eight acrocentric chromosomes. The presence of only two metacentric chromosomes is the result of preferential exclusion of human chromosomes[12,13]. The possibility remains that one or more telocentric chromosomes in the hybrid may be of human origin.

This hybrid clone secretes both human and mouse Igs. We have found no evidence of exclusion of synthesis or of secretion of either Ig in the hybrid cells. Individual cells synthesize and secrete both human and mouse Igs. The three radioactivity peaks on SDS gels, of hybrid medium precipitated with antiserum to human Ig, co-migrating with H_2L_2, H_2 and L_2, indicate either that some of the human Ig is IgA, in which H_2 and L_2 are non-covalently bound together, and/or that hybrid antibody is synthesized by these cells.

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Transplantation of Isolated Pancreatic Islets into the Portal Vein of Diabetic Rats

RECENT work from this laboratory indicates that intraperitoneal transplantation of isolated pancreatic islets ameliorates the effects of experimental diabetes in rats[1] Although the intraperitoneal siting of these islets reduces the hyperglycaemia and polyuria of streptozotocin induced diabetes in these animals, consistently normal values for blood sugar and urine volume are rarely achieved

In normal circumstances, insulin from the pancreatic β-cells is secreted directly into the portal venous system and we have investigated the possibility that this intraportal site may provide a more physiological environment for the transplanted islets and possibly more effective use of secreted insulin

Pancreatic islets were collected from Lewis rats by the collagenase digestion method of Lacy and Kostianovsky[2] and separated from unwanted acinar debris by differential layering of dialysed 'Ficoll'[3] This technique involves the mixing of digested pancreas with 'Ficoll' 25% (w/v) and the careful layering above this mixture of 'Ficoll' in decreasing concentration (23%, 20% and 11%) Centrifugation for 10 min at 800*g* leaves the acinar tissue in the 25% 'Ficoll' while islets rise through the density gradient to settle at the 20–11% interface The isolated islets (400–600) were then injected through a 1 ml siliconized syringe and No 23 needle into the portal vein of diabetic Lewis rats of the same inbred strain as the donors Diabetes had been induced in these recipient rats 3 weeks before by the intravenous injection of streptozotocin (65 mg kg^{-1}) and the study included a group of ten diabetic rats as control animals

After the transplantation operation all rats were returned to their metabolic cages and observed for 4 weeks during which a free diet of rat chow and water was allowed Urine volumes were measured daily and blood glucose levels estimated on alternate days

The ten control animals were grossly diabetic with blood glucose levels varying between 270 and 720 mg/100 ml and urine volumes between 80 and 150 ml daily Direct injection of pancreatic islets into the portal vein resulted in normoglycaemia and normal urine volumes in the five rats studied (Fig 1)

These results suggest that if transplantation of isolated pancreatic islets is to be used in the treatment of clinical diabetes the portal venous system may be the site of choice for maximal effectiveness

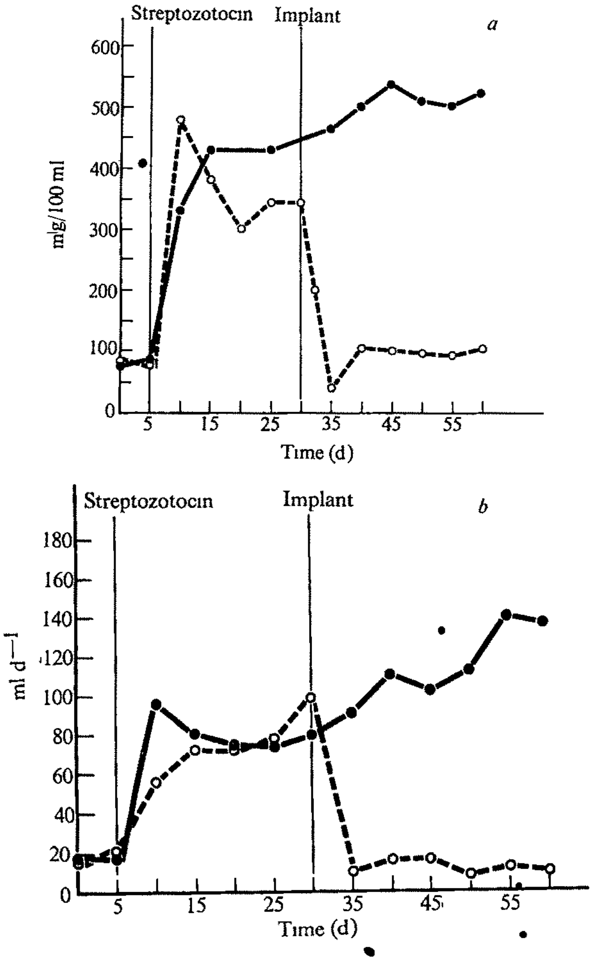

Fig 1 Effect of portal vein implantation of pancreatic islets on the blood glucose (*a*) and urine (*b*) volumes of diabetic rats (Mean of ten diabetic controls and five portal vein implants) Values after transplantation diabetic controls (●) blood sugar 270 to 720 mg%, urine volumes 80 to 150 ml daily, portal vein implant (○) blood glucose 66 to 140 mg%, urine volume 6 to 20 ml daily

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Sulphate Conjugation and L-Dopa Treatment of Parkinsonian Patients

CONJUGATION of catecholamines in man was first described for adrenaline by Richter in 1940[1] He suggested that the conjugated product was an ester of sulphuric acid Richter and MacIntosh[2] later demonstrated that conjugation of adrenaline markedly reduced its pressor properties and proposed that conjugation is a mechanism of inactivation of the biological properties of this amine Holtz and Credner[3] administered L-dopa to several animals including man and isolated both free and conjugated dopamine (DA) from urine Conjugation of two metabolites of DA, homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC), was observed by Shaw, McMillan and Armstrong[4] when they isolated these two phenolic acids from the urine of human subjects who had received L-dopa orally The conjugates of these compounds can be isolated by anion exchange chromatography[5,6] When conjugated derivatives in the eluates from anion exchange columns were hydrolysed by sulphuric acid[5,6] or sulphatase[5], the unconjugated parent compounds were identified by paper chromatography

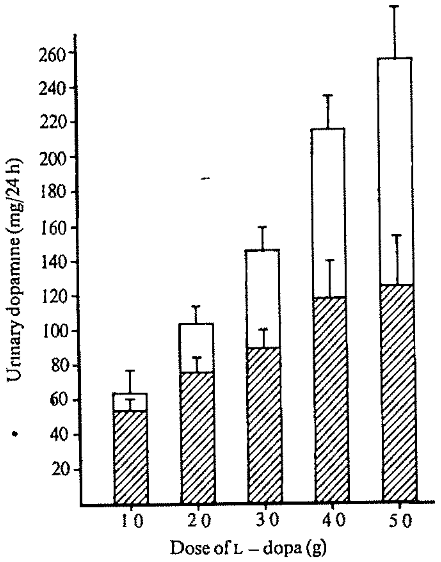

Fig. 1 Urinary excretion of DA from Parkinsonian patients treated with increasing dosages of L-dopa. Each value represents the mean ±s.e.m. of conjugated (▨) and nonconjugated (☐) DA excreted (mg per 24 h).

Richter[1] suggested that sulphate conjugation might be limited with large amounts of phenolic substrate, and studies in rabbits indicate that conjugation of phenolic compounds with sulphuric acid is reduced as the dose of the phenolic substrate is increased[7,8]. Because of the large doses of L-dopa employed in the treatment of Parkinsonian patients[9,10], it is possible that sulphate conjugation of DA and its metabolites will be reduced as the dosage of L-dopa is increased. An enhancement of the therapeutic effect of L-dopa with increasing dosages may be due to a reduction of conjugation with a consequent elevation of free DA. It is the free DA which is presumably responsible for many of the therapeutic and toxic effects of the drug. The purpose of this investigation was to study sulphate conjugation of DA and metabolites of DA with increasing dosages of L-dopa in patients with Parkinsonism.

Eight women and seven men with Parkinsonism were withdrawn from previous medication for at least a week before the study. The patients were aged from forty-nine to eighty-three with a mean age of sixty-seven. The duration of the disease in the twelve patients with primary Parkinsonism ranged from 3 to 13 yr (a mean duration of 7 yr) and the disease had been evident in the three patients with postencephalitic Parkinsonism for 8, 35 and 36 yr. Seven patients had severe and disabling disease (stages IV and V). Eight patients had mild to moderate disease and were still independent in their activities of daily living (stages II and III). The patients were admitted to a clinical research ward, and at least one 24 h urine sample was obtained before beginning therapy with L-dopa. The diet was not controlled except that foods containing catecholamines were restricted[11,12]. L-Dopa treatment was started as 1.0 g d^{-1} in four divided doses. The dosage was increased by 0.5 g d^{-1} every 2 d to a dose of 3.0 g d^{-1}. The patients were discharged from the hospital and the dosage was increased by 0.5 g d^{-1} every 1 to 2 weeks to a total daily dosage of 3.0 g d^{-1} in two patients, 4.0 g d^{-1} in three patients, and 5.0 g d^{-1} in ten patients. Twenty-four hour urine samples were collected at the end of each dosage interval in bottles which contained 2.0 g sodium metabisulphite as a preservative. An aliquot of the urine was hydrolysed by boiling with hydrochloric or sulphuric acid[13]. Some samples were also hydrolysed enzymatically with glusulase as described by Smith and Weil-Malherbe[14]. No differences in the values of metabolites could be detected following the different methods of hydrolysis. Dopa, DA and DOPAC were isolated from urine of treated patients by alumina chromatography[15] and were separated and assayed by paper chromatography according to the method of Sourkes[16]. DOPAC from the urine of untreated patients was also determined by this procedure. To attain the greater specificity and sensitivity required for assay of DA, the method of Anton and Sayre[15] was employed for urine from untreated patients. Dopa could not be detected consistently in the urine of untreated patients. HVA was determined by a modification of the procedure of Sato[17]. This method involves the isolation of HVA on 'Dowex' 1, an anion exchange resin, and elution with 18 ml of 2 N HCl. HVA is converted to a fluorescent product by oxidation with potassium ferricyanide. The urinary content of each metabolite was corrected for recovery. The recoveries were (mean ± s.e.m.) dopa, 72.1±4.0%, DA, 76.0±4.0%, DOPAC, 54.6±2.7%, and HVA, 74.0±4.7%. When urine samples were to be analysed for sulphate, hydrolysis was attained by boiling the urine with hydrochloric acid as described by Hawk, Oser and Summerson[18]. The glusulase method of hydrolysis[14] was also used in a few experiments and similar results were obtained. Sulphate was determined in hydrolysed and nonhydrolysed urine samples by the turbidimetric procedure of Berglund and Sorbo[19].

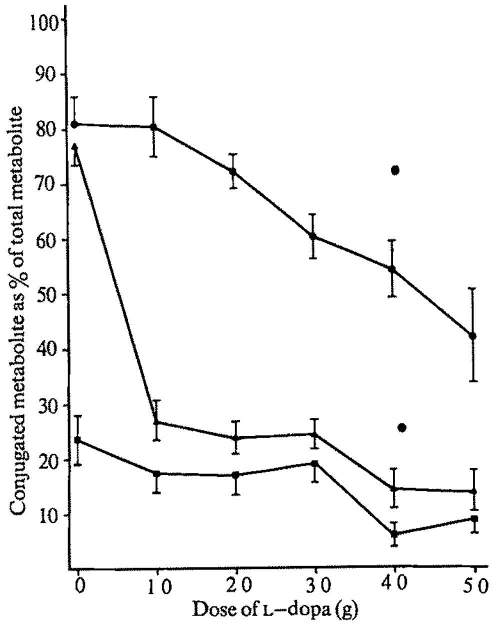

Fig. 2 Conjugation of urinary DA (●), DOPAC (▲) and HVA (■) with increasing dosages of L-dopa. The values represent the mean ± s.e.m. of % conjugation of the metabolite.

The excretion of DA in urine of untreated Parkinsonian patients amounted to 94±21 (s.e.m.) μg per 24 h. The amount of DA found in the urine of these patients increased to 659±93 μg per 24 h after the hydrolysis procedure. Thus, approximately 80% of the total DA was conjugated. When 1.0 g of L-dopa was administered, the excretion of DA increased markedly so that a total of 61.6±7.6 mg per 24 h was excreted from hydrolysed urine (Fig. 1). The proportion of the total conjugated DA did not differ from that observed in the untreated patients. As the dosage of L-dopa was increased, the total DA excreted in the urine increased proportionally and the free DA represented a progressively greater fraction of the total. This can also be seen in Fig. 2 where the conjugation of DA is compared to the conjugation of DOPAC and HVA with increasing dosages of L-dopa. DOPAC excretion in the absence of L-dopa treatment was 321±51 μg per 24 h in nonhydrolysed urine and 1,683±183 μg per 24 h in hydrolysed urine. HVA excretion was 2,630±310 μg per 24 h in nonhydrolysed urine and 3,324±366 μg per 24 h in hydrolysed urine. After treatment with L-dopa, the excretion of total DOPAC and HVA (from hydrolysed urine) was proportional to the dose of dopa and represented 230±10.6 mg DOPAC g^{-1} of dopa administered per 24 h and 265±12 mg HVA g^{-1} of dopa administered per 24 h. The conjugation of

DOPAC and DA occurs to approximately the same extent but HVA is conjugated to a much smaller degree After L-dopa administration, the % of DOPAC which was conjugated was reduced This was observed with much smaller dosages of L-dopa than were required to decrease the proportion of conjugated DA Conjugation of HVA was relatively unaffected until 4 0 to 5 0 g d^{-1} of L-dopa was administered As dopa was not consistently demonstrable in urine from untreated patients, the conjugation of endogenous dopa could not be estimated Conjugation of dopa in three untreated patients was determined by administering 28 2 mg of ^{3}H-L-dopa (200 µCi, 1 4 Ci $mmol^{-1}$) orally and measuring ^{3}H-dopa in hydrolysed and nonhydrolysed urine samples It was observed that 90 6±4 2% of the ^{3}H-dopa in the urine was conjugated When the fifteen patients were treated with L-dopa, total dopa (from hydrolysed urine) was excreted in proportion to the dosage of L-dopa and represented about 5 5 mg g^{-1} of L-dopa administered per 24 h Of this amount, about 25% was conjugated at all dosages of L-dopa

The metabolites of L-dopa are thought to be conjugated as sulphates and the organic sulphate excreted in the urine may be expected to increase Indeed, both the organic sulphate and the proportion of total sulphate in the organic form was increased with increasing dosages of L-dopa (Fig 3) The total sulphate (organic and inorganic) excreted was not markedly changed with increasing dosage of L-dopa and averaged 2 43±0 14 g per 24 h Glucuronic acid was also determined to obtain an index of glucuronide conjugation of L-dopa and its metabolites Total glucuronic acid was determined colorimetrically by the method of Maughan, Evelyn and Browne[20] In untreated patients, total glucuronic acid excretion amounted to 357±59 mg per 24 h This was not changed upon administration of L-dopa This is indirect evidence that glucuronic acid is not primarily involved in conjugation of metabolites of L-dopa as total glucuronic acid is known to increase when it is conjugated with large amounts of phenolic substrate[21]

To confirm that the conjugation of DA was primarily with sulphuric acid, the sulphate conjugate of DA was isolated by anion exchange chromatography on 'Dowex' 1 according to the method of Goodall[6] The material which was eluted where the DA sulphate would be expected was hydrolysed with hydrochloric acid and assayed for DA by the procedure of Anton and Sayre[15] No DA was detected in this fraction before hydrolysis The content of DA sulphate analysed in this manner corresponded well to the content of DA analysed in hydrolysed and nonhydrolysed urine without previous isolation on the 'Dowex' 1 column The eluate which corresponded to the DA sulphate fraction of the 'Dowex' 1 column was also analysed by infrared spectrometry and the spectrum was identical to that of authentic DA sulphate

The excretion of DA and its metabolites after therapy with L-dopa has been measured in numerous studies but little attention has been given to the sulphate conjugation of these substances Cotzias *et al* [9] observed that the excretion of free DA was not proportional to the dosage of L-dopa, but rather that the % of L-dopa excreted as free DA increased linearly as the dosage of L-dopa was increased Their results were similar to those of this study in that the proportion of free DA increased with increasing dosages of L-dopa The data from this study indicate that this can be explained by a decrease in the % of conjugated DA with large dosages of L-dopa

The decrease in the % of DA sulphate excreted could be the result of either increased sulphatase activity or decreased sulphate conjugation There is evidence to indicate that the latter may be the more significant Bray *et al* [22] demonstrated in the rabbit that the level of endogenous inorganic sulphate is normally rate limiting in the formation of arylsulphates *in vivo* On the administration of such substances as phenol[7] and adrenaline[8] there is a dose-related decrease in the proportion of the conjugated product

The source of endogenous sulphate seems to derive from the catabolism of protein rather than from the diet Young and Maw[23] have shown that cystine is the major source of sulphate used in ethereal sulphate synthesis It is clear that the total sulphate cannot be rate limiting as the rate of sulphate conjugation is markedly reduced with 5 g of L-dopa and yet only 45% of the total sulphate in the urine is present as organic sulphate Thus, it is probable that the pool of sulphate available for conjugation does not freely equilibrate with total body sulphate and it is the sulphate pool available for conjugation which becomes rate limiting

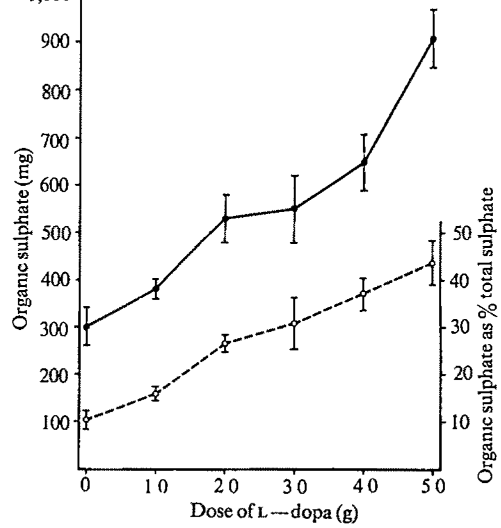

Fig. 3 Urinary excretion of organic sulphate with increasing dosages of L-dopa Values are expressed as either mg of organic sulphate per 24 h ± s e m (sulphate in hydrolysed urine—sulphate in nonhydrolysed urine) (●—●) or % organic sulphate ±s e m (○— — —○)

Preliminary evidence from this laboratory on the metabolism of ^{3}H-L-dopa given orally and intravenously suggests that conjugation of dopa and its metabolites takes place predominantly in the intestine Other studies have shown that adrenaline[24] and isoproterenol[25] are conjugated to a greater extent after oral than after parenteral administration It is also known that the intestinal wall as well as the liver is capable of sulphate conjugation[26] Sulphate conjugation of phenolic biogenic amines and amine metabolites is also known to take place in the brain[27–29] If suppression of conjugation occurs in the brain this would result in more free DA being available to exert a therapeutic or toxic effect There is indirect evidence that changes in behaviour are related to free DA rather than to conjugated or total DA Weil-Malherbe and Van Buren[11] observed that free DA in the urine of Parkinsonian patients was markedly reduced when compared to controls, but that conjugated DA in Parkinsonian patients was not significantly different from that of healthy subjects Similarly, Mattock *et al* [30] observed that free DA was reduced in the urine of schizophrenic patients, but that conjugated DA was not significantly different from that of normal subjects Preliminary analyses of the patients of this study suggest that the rigidity ($P<0$ 005) and akinesia ($P<0$ 010) in the untreated patients correlate negatively with free DA in the urine but are not correlated with conjugated or total DA in the urine

The results of this study suggest that high dosages of L-dopa reduce the rate of sulphate conjugation of DA allowing for marked increases in the free DA which may be available to produce its therapeutic as well as its toxic effects

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Isolation of a Factor from Human Seminal Plasma that Promotes Fertilization

EXTENSIVE studies on the seminal plasma of man and other species have attempted to define the role of various components on the metabolism of spermatozoa, on the female reproductive tract and on the motility of spermatozoa and their capacity to fertilize the ovum[1-7] These studies have provided evidence of a role for fructose, cyclic AMP, prostaglandins and other constituents[1,8] We report here a newly discovered small molecular weight substance in human seminal plasma with a beneficial effect on the fertilization by epididymal sperm of ova of two mammalian species

Seminal plasma of normal human males was pooled and centrifuged at 1,440*g* for 30 min The supernatant was again centrifuged at 30,000*g* for 45 min The clear seminal fluid obtained was chromatographed on a 'Sephadex' G-15 column, and eluted with 20 mM ammonium bicarbonate (Fig 1)

Of the five fractions, fraction III was collected from different runs, pooled and lyophilized The residue was taken in distilled water and lyophilized This process was repeated three or four times to remove the ammonium bicarbonate added The solid residue was reconstituted in a small volume of distilled water Further separation of fraction III was carried out by paper chromatography (see legend to Fig 2) The paper was then sprayed with diazo reagent[9], which gives evidence of primary, secondary or tertiary amino groups, as well as phenolic groups in the molecule A compound staining light orange was obtained that is denoted as P (promoter) factor It was eluted with water, freeze dried and stored at 4° C

The effect of P factor was tested on fertilization in rabbits and mice The action on *in vivo* fertilization in rabbits was assessed by the procedure described previously[10] Sperm from the cauda epididymis of a male rabbit were collected in Krebs-Ringer phosphate buffer, *p*H 7 4, supplemented with 5 mg ml^{-1} glucose and 5% heated (56° C, 30 min) rabbit serum (KRPGS) The sperm were capacitated by injection into the uteri of a virgin doe primed with 75 IU of HCG (Ayerst Lab) After 12 h the uteri were flushed with KRPGS The suspension of capacitated sperm was diluted to 4 to 6×10^5 sperm ml^{-1} and was divided into two parts P factor (250 µg ml^{-1}) was added to one and the other received an equivalent volume of the vehicle, both were incubated at 37° C for 20 to 30 min Superovulation was induced in mature virgin does by injecting 170 IU of PMS (Sigma) subcutaneously, followed 72 h later by 150 IU of HCG intravenously After 15 to 16 h of HCG administration, capacitated sperm with or without test substance were inseminated into the oviducts One fallopian tube of each rabbit received 0 05 ml of treated sperm suspension and the other received 0 05 ml of untreated sperm suspension (control) The fallopian tubes were flushed with 0 9% saline 26 h later The ova were collected and examined for fertilization, ovulation points were also counted on the ovaries Figures 3*a* and *b* show the typical appearance of fertilized and unfertilized ova at this stage

Table 1 Effect of P Factor on *in vivo* Fertilization of Rabbit Ova

Test substance	No of oviducts examined	Ova fertilized/ Total number of ova	Ova fertilized* (%)
None, control	20	95/190	50
250 µg ml^{-1} P factor	20	172/200	86

*$P<0\ 001$

Table 1 summarizes the results of the effect of P factor on fertilization of rabbit ova Of 200 ova 86% were fertilized and

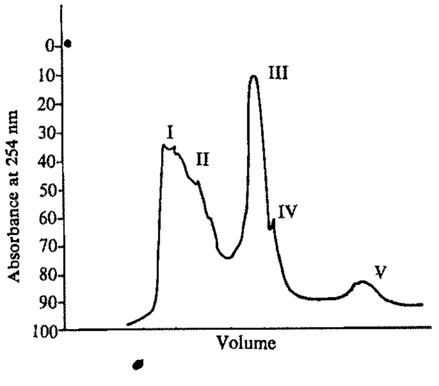

Fig 1 Fractionation of human seminal plasma on 'Sephadex' G-15 column (3×80 cm), clear seminal fluid (10 ml) was loaded Elution was carried out with 20 mM NH_4HCO_3 Flow rate was adjusted to 1 5 ml min^{-1} The profile was recorded by an automatic LKB fraction collector, fitted with uv cord to monitor the absorbance continuously at 254 nm

Table 2 Effect of P Factor on *in vitro* Fertilization of Mouse Ova

Test substance	Amount of P factor (μg)	Ova fertilized/ Total number of ova	Ova fertilized (%)
Experiment I			
Control (0.5 ml sperm suspension)	—	1/33	3
+P factor	40	15/27	55
	80	12/16	75
	120	24/30	80
	160	28/31	90
Experiment II			
Control (0.5 ml sperm suspension)	—	2/17	12
+P factor	40	5/20	25
	80	12/23	50
	120	6/9	66
	160	14/15	93
Experiment III			
Control (0.5 ml sperm suspension)	—	8/18	44
+P factor	40	12/24	50
	80	14/20	70
	120	19/23	83
	160	17/19	90

appeared to have undergone normal cleavage and development to the four- or eight-cell stage in the treated group compared with control oviducts in which of 190 ova shed 50% were fertilized.

Experiments were extended to another species to see whether P substance affected fertilization in ova other than from rabbits. The fertilization of mouse ova was studied *in vitro* using the procedure of Miyamoto and Chang[11], with slight modifications. Superovulation was induced in five mature Swiss albino mice by an intraperitonial injection of 5 IU of PMS followed 44 to 48 h later by 5 IU of HCG. The mice were killed at 14 to 16 h after the injection of HCG. The oviducts were removed and placed under paraffin oil in a watch glass at 37° C. Eggs in the cumulus clot were released into the oil. The paraffin oil, sublayered with a small volume of sterile saline, was equilibrated with 5% CO_2 in 95% air. The sperm suspension was prepared by mincing cauda epididymis of a mature Swiss albino mouse in a watch glass containing 5 ml of the medium[12]. Aliquots of 0.5 ml of sperm suspensions (1 to 5×10^6 sperm ml^{-1}) were incubated with 40, 80, 120 or 160 μg of P factor for 20 to 30 min at 37° C. Sperm suspensions with and without treatment were added to separate watch glasses containing the ova under paraffin oil. After incubation at 37° C for 5 to 6 h, the eggs were removed and washed in 2 ml of culture medium. They were then transferred to a culture medium of the same composition as that used by Whitten and Biggers[13], except that the concentration of sodium pyruvate was 0.55 mM. The medium was layered with paraffin oil. After 24 h, the eggs were examined for fertilization and cleavage (Figs 3*c* and *d*).

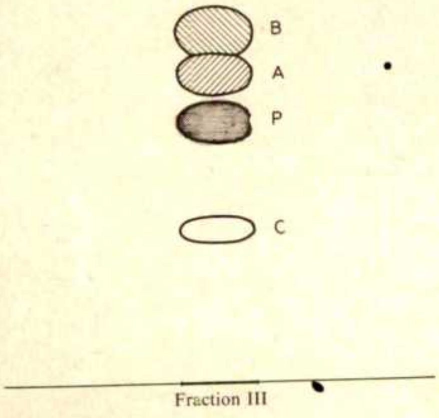

Fig. 2 Fraction III was further resolved by descending paper chromatography on Whatman Paper No. 1. The solvent system was *n*-propanol : 1 N acetic acid (3 : 1). Spots A, B and C show absorption in ultraviolet light. P is the "promoter factor", staining light orange with diazo reagent[9].

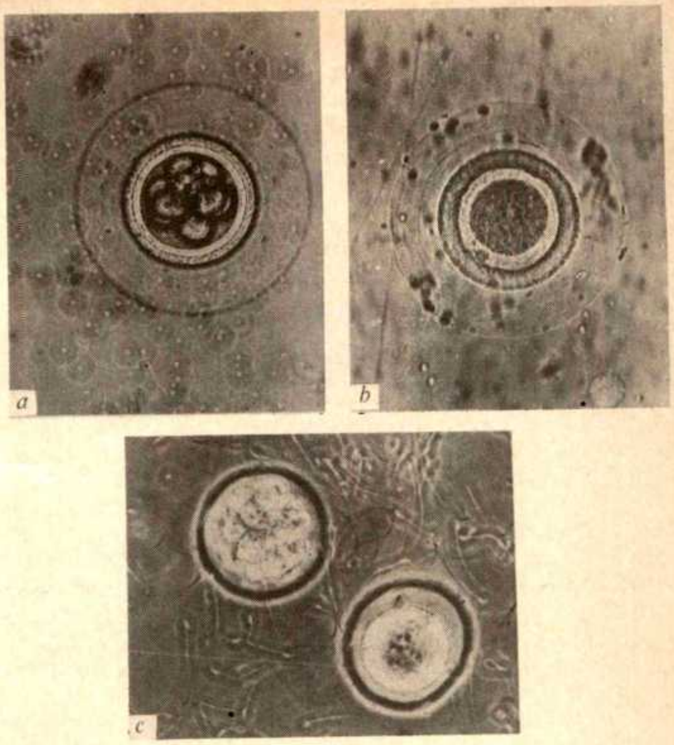

Fig. 3 *a*, Fertilized rabbit ovum at eight-cell stage; *b*, unfertilized rabbit ovum; *c*, mouse ovum fertilized *in vitro* at eight-cell stage; *d*, unfertilized mouse ovum.

The results are given in Table 2. The % ova fertilized varied considerably in the control group (3 to 44%). Treatment with P factor substantially increased the number of ova fertilized. Data further show that with the increase in concentration of P substance, the number of ova fertilized increased progressively such that 93% of eggs were fertilized in the presence of 160 μg/0.5 ml of P factor. This substance has thus a notable influence on the fertilization of ova from two mammalian species. Although the substance is of human origin, experimental limitations did not permit its testing in humans. It is not unlikely, however, that P factor has a role in promoting fertilization in human and other species.

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Zirqa Virus, a New Arbovirus isolated from Bird-infesting Ticks

In October 1968, the Department of Entomology at the London School of Hygiene and Tropical Medicine received from the Chief Medical Officer of the British Petroleum Company Ltd, two nymphs of an argasid tick. They were collected from the island of Zirqa (Zarrakkuh) (24°53′N, 53°04′E) off the coast of Abu Dhabi in the Persian Gulf and were associated with ground-nesting ospreys (*Pandion h. haliaetus*) and Socotra cormorants (*Phalacrocorax nigrogularis*) which appear on the island towards the end of August and remain till early February. The island is barren and uninhabited by humans. Abu Dhabi Marine Areas Limited (ADMA) have a radiomast and generator on the island and ADMA personnel make regular visits for routine maintenance of the plant. Local fishermen also visit the island from time to time. Attention was drawn to the presence of ticks when personnel were bitten by them and reacted with allergic symptoms, septic sores and high temperature. Case history notes are given by Hoogstraal, Oliver and Guirgis[1]. Blood smears from a patient who was ill following tick bites were negative for spirochaetes, protozoa and microfilariae. The ticks were identified by one of us (M. G. R. V.) as *Ornithodoros* sp. and sent to Dr H. Hoogstraal of NAMRU-3, Cairo, who assigned them to *Ornithodoros* (*Alectorobius*) *muesebecki* described from specimens collected from a booby colony on Hasikiya Island, South Yemen Republic, in the Arabian Sea[2].

In November 1969, several specimens of this tick collected from the nests of cormorants on Zirqa Island by the late Dr R. M. Oliver, Senior Medical Officer of the British Petroleum Company, were received. Because it seemed possible that the symptoms in humans following tick bites had a viral aetiology, the ticks were processed for virus isolation.

Twenty-five nymphs of all stages were killed by chilling 2 d after receipt and ground up in 2 ml of 0.75% bovine albumin in borate buffered saline at *p*H 9 (BABS) with 1,000 U of penicillin and 1 mg of streptomycin ml^{-1}. After centrifugation, the supernatant fluid was inoculated into two litters of eight 1-d-old white mice (TO strain), each mouse receiving 0.02 ml intracerebrally and 0.03 ml subcutaneously. The rest of the tick suspension was stored in sealed glass ampoules at −60° C. One litter was lost through the mother's eating the babies. Eleven days after inoculation, two of the mice in the second litter were paralysed and three were ill. A 10% brain suspension in BABS from two of the ill mice was inoculated intracerebrally into a further four litters of 2-d-old mice. A broth culture of the brain suspension was negative. The isolate in the second passage in suckling mice had an incubation period of 6 d. Third passage mouse brain suspension of the prototype strain (A2070-1) had an intracerebral titre of 7.0 log per 0.02 ml in suckling mice. The agent was pathogenic to adult mice also and the incubation period in 3 to 4-week-old mice inoculated intracerebrally with 10^{-4} dilution of third passage suckling mouse brain suspension was 6 d. Third and fourth passage mouse brain suspensions titred 5.9 log to 6.5 log per 0.03 ml intracerebrally in adult mice. The agent has been named Zirqa virus. The virus has been re-isolated from the original tick suspension after more than 3 yr storage at −60° C and the identity of the isolate confirmed by complement fixation tests. Additional strains of the virus were also isolated from ticks sent to NAMRU-3, Cairo, by Dr R. E. Williams.

Further tests done at the Microbiological Research Establishment at Porton (D. I. H. S. and E. T. W. B.) showed that the mouse intracerebral LD_{50} of the agent was reduced by 3.4 log after treatment with an equal volume of ether at 4° C for 1 h and by ≥4.6 log after treatment with a final concentration of 0.1% sodium deoxycholate at 37° C for 1 h. An antigen prepared from third passage mouse brain suspension after sucrose-acetone extraction, sonication and trypsin and protamine treatment and tested in haemagglutinin inhibition (HI) tests against antisera to selected arboviruses showed that the agent did not belong to arbovirus serological groups A, B, Bunyamwera, Simbu, California, Kaisodi or Bakau.

A screening complement fixation test done at the Yale Arbovirus Research Unit (J. C.) with immune serum for Zirqa virus and all antigens from non-group B tick-borne viruses to hand (about 40) established the virus as a new agent in the Hughes group of tick-borne arboviruses, closer to Farallon than to the other viruses of the group (Table 1).

Table 1 Relationship between Zirqa Virus and Other Members of the Hughes Group as Determined by Complement Fixation Tests

Antigen	Serum Zirqu	Farallon	Punta Salinas
Zirqa (A2070–1)	512/128*	64/64	1:8
Farallon	64/512	512/512	1:32
Hughes	16/16+		1:32
Soldado	16/16		1:8 traces
Punta Salinas (Cal Ar 888)			1:128
Normal	0/0	0/0	0

* Reciprocal of serum titre/reciprocal of antigen titre.

All the viruses in the Hughes group, including Zirqa, are associated with marine birds and *Ornithodoros* spp. The investigation of similar biocenoses elsewhere may reveal the existence of other viruses. There is no known human illness associated with Farallon, Hughes or Soldado viruses. Punta Salinas isolated from *Ornithodoros amblus*, a species closely related to *O. muesebecki*, has been identified as a member of the Hughes group (H. Johnson, personal communication). Dr Johnson informs us that this virus and another, Huacho virus, belonging to the Kemorovo-Chenuda group, may be likely candidates for the febrile illness associated with tick bites that occurs among guano workers off the coast of Peru. On Zirqa Island, the ticks appeared within a matter of minutes on the nearby ground surface when a person placed a bare foot near cormorants' nests and some dexterity was required to avoid being bitten[1]. There is no clear evidence so far that Zirqa virus was the aetiological agent of the illness among the petroleum industry workers on Zirqa Island, but the isolation of this virus underlines the potential danger to man when he makes effective contact with such silent foci of infection.

We are grateful to the late Dr R. M. Oliver and to Dr J. G. Clothier, Chief Medical Officer of the British Petroleum Company Ltd, for bringing our attention to the tick and for much of the information about the island and the tick.

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Form and Role of Deformation in Excitation of an Insect Mechanoreceptor

THE proprioceptive campaniform sensilla of insect legs are thought to sense strains developed in the cuticle of the leg in weight bearing and walking. Pringle[1] proposed that a ridge in the cuticular cap of the sensillum bulges outward under compressional shear stress, thus stretching and exciting the underlying single bipolar sensory neurone. His main assumption was that the mechanical compliance of the cuticle should differ in at least two subregions of the cap. This hypothesis has been widely accepted and is probably substantially correct, but several essential details have not been tested directly. Until now, the structure of the cap has not been shown clearly in cockroach legs, although it has been in dipterous halteres[2,3], and neither the mechanical properties of the cap cuticle nor the magnitude and direction of the excitatory deformation have been measured, although the fine structure of the bipolar neurone[4,5] and its responses to punctate stimulation[6,7] are known.

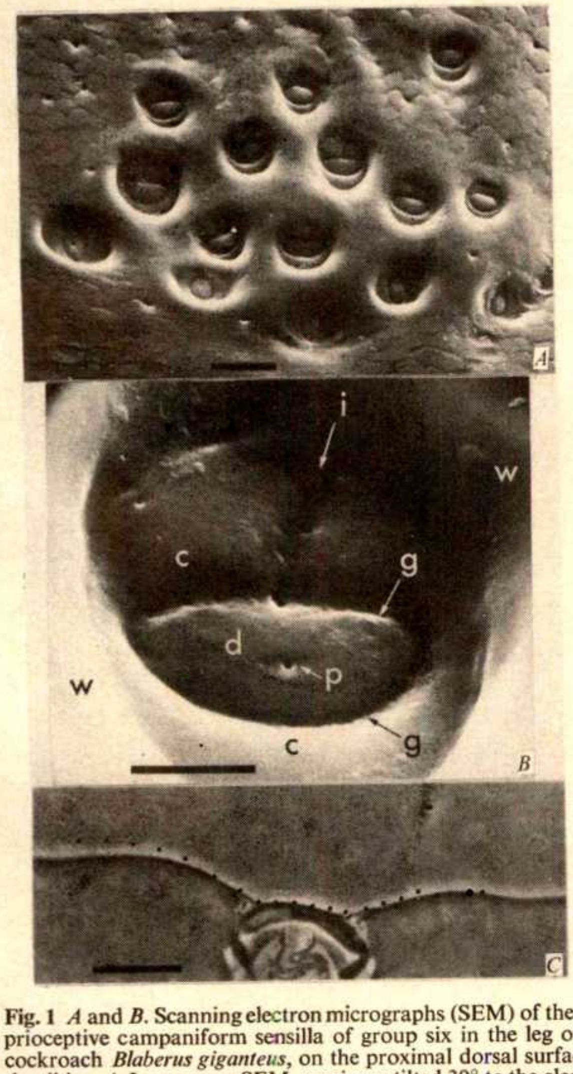

Fig. 1 *A* and *B*. Scanning electron micrographs (SEM) of the proprioceptive campaniform sensilla of group six in the leg of the cockroach *Blaberus giganteus*, on the proximal dorsal surface of the tibia. *A*, Low power SEM, specimen tilted 30° to the electron beam. Fifteen sensilla are seen recessed beneath the tibial surface in crater-like depressions. The top of the picture is proximal. Scale, 20 µm horizontally, 23 µm vertically. *B*, High resolution SEM of a single sensillum oriented as *A*. Convex oval dome, *d*, is separated by narrow groove, *g*, from the thin surrounding cap cuticle, *c*, which joins the thick walls of the crater, *w*. Pit, *p*, formed around the old sensory process before ecdysis at the last moult. Irregular depression, *i*, is proximal to the dome regardless of the dome's orientation. Scale, 5 µm horizontally, 5.8 µm vertically. *C*, Phase micrograph of the section through the major axis of the sensillum of Fig. 2, comparing the anatomic contour of the cuticle with that measured by the stimulating probe. Points are those of Fig. 2, "surface elevation", left. Sensory process and other non-cuticular tissue was not preserved. Scale, 10 µm.

We describe here the surface structure of these sensilla as revealed by the scanning electron microscope, and the mechanical compliance, surface deformation and sensitivity as measured by a new application of punctate mechanical stimulation. All work was done with the campaniform sensilla of Pringle's[1] tibial group six. Scanning electron micrographs were taken in the cockroach *Blaberus giganteus* and the physiological measurements in *B. discoidalis*. A preliminary report has been presented[8].

Fig. 1*A* shows, at low magnification, the caps of fifteen sensilla of group six recessed a few micrometres into the surface of the tibia. A single cap comprises a directionally orientated convex oval dome located within a crater-like depression (seen at high magnification Fig. 1*B*). The dome, decorated by a tiny, centrally-located moulting pit[9,10], sits in a narrow groove which defines its perimeter, and is slung from the walls of the crater by a thin, curved field of exocuticle. A narrow, irregular depression, probably formed by the underlying enveloping cell, runs proximally from the edge of the dome to the edge of the cap. The proprioceptive campaniform sensilla of cockroach legs thus differ substantially from their counterparts on the halteres of flies[2,3]. The convex oval dome evidently accounts for the central ridge seen with transmitted light in potashed preparations[1].

In a series of punctate mapping experiments, forces up to 10 dynes were applied to the larger campaniform sensilla with a tungsten probe of 1 to 2 μm tip diameter, attached to a piezoelectric ceramic bender mounted on an electric resistance force gauge. While observing with a ×600 microscope, the probe was positioned over the sensillum manually with a micromanipulator, but lowered onto it electrically by a d.c. voltage applied to the bender. The bender voltage thus measured the vertical contour of the surface as a precise indicator of probe location (Fig. 1*C*, points) and also determined the applied force. In addition, a superimposed a.c. voltage at 3 Hz modulated the contact force by 2 to 4 dynes. At responsive points on the cap, the sensory neurone produced modulated bursts of several nerve impulses per cycle, monitored as 100 to 300 μV spikes from pin electrodes through the femur. A PDP-12 computer was used on-line to average the waveforms of bender voltage, contact force, and impulse frequency (as pulse time density), and off-line for subsequent calculations.

As the probe was moved from point to point on the cuticular surface, variations occurred in the modulated force F developed per volt of a.c. signal V applied to the bender $(\partial F/\partial V)_s$, due to variations in the compliance C_s of the cuticular surface. We could thus use $(\partial F/\partial V)_s$ to measure not only the compliance, but also the indentation produced by the stimulus. Surface compliance C_s was obtained as:

$$C_s = B/(\partial F/\partial V)_s - C_P$$

in which B, the free deflexion of the probe tip per volt applied to the bender, and C_P, the compliance of the probe assembly, are independently measured properties of the apparatus. Surface indentation ΔZ was determined from the force and the compliance as:

$$\Delta Z = \int_0^F C_s \, dF$$

Minimum thresholds for indentation, which occurred at the centre of the dome, were 10 to 20 nm, of the order of 0.03% of the combined length of the dendrite and sensory process of the bipolar neurone[4]. Force sensitivity (impulse frequency modulation per unit force modulation) displayed a broad peak along the major axis of the dome (Fig. 2) and a sharper peak along its minor axis. Indentation sensitivity (force sensitivity divided by compliance) peaked even more sharply,

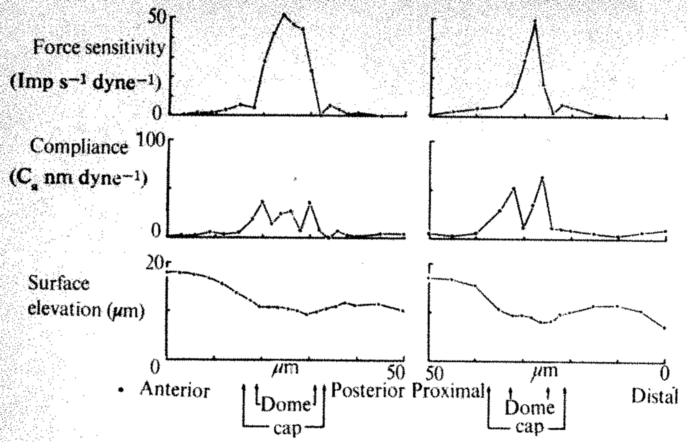

Fig. 2 Profiles of sensitivity, compliance and surface contour from mapping measurements on the major (left) and minor axis (right) crossing the centre of a large transversely orientated sensillum of *B. discoidalis*. High sensitivity to contact force and indentation is restricted to the midline of the dome, while compliance maxima occur on the surrounding groove.

with a maximum of 2 to 5 impulse s^{-1} nm^{-1} at the centre of the dome. The most sensitive region of the cap for stimulating the sensillum, the midline of its long axis, thus corresponds to the position of insertion of the flat, paddle-shaped tip of the sensory process[4,5]. Greatest compliance, however, occurred at the edges of the dome, forming a ring around it. This suggests that the dome is a relatively hard object suspended on a soft gasket. It probably tilts when probed at its edges, but indents uniformly when probed at its centre. Tilting is thought to excite insect hair sensilla by pinching[11] or bending[12] the sensory process, but this is evidently a weak stimulus for proprioceptive campaniform sensilla.

We therefore support Pringle's hypothesis[1] in that the compliance of the cap cuticle surrounding the dome differs indeed from that of the dome itself. Gently indenting the dome, however, is an extremely effective experimental stimulus and should compress the sensory process longitudinally into the dendrite, rather than to stretch[1], pinch[11], or bend[12] it. We suggest, therefore, that the cuticular strains produced physiologically during proprioception excite the campaniform sensillum in this way by indenting its dome by a few tens of nanometres.

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Normal Development of Mechanically Activated, Unlaid Eggs of an Endoparasitic Hymenopteran

In the Ichneumonid wasp *Pimpla turionellae*, as in many other Hymenoptera, males develop from unfertilized eggs with a haploid set of chromosomes. Thus, fertilization of the egg is not necessary for its activation. During our investigations on egg development in *Pimpla*[1–5] the question arose as to what actually causes the conclusion of meiosis and initiation of cleavage in the oocyte nucleus after oviposition, and also what induces the beginning of the characteristic morphogenetic movements of the ooplasm in initial regions[5].

In *Pimpla*, the diameter of the ovipositor egg canal (less than 60 μm in its distal part) is much smaller than the width of a fully grown egg (on average 260 μm at the widest point). This implies that on its way through the ovipositor the egg must be squeezed firmly. We assumed that the mechanical deformation of the egg alters the egg architecture and thus induces the beginning of embryonic development, for undeformed eggs explanted from the ovarioles of imagos ready to oviposit do not develop. The correctness of this assumption has now been proved by the demonstration that explanted eggs which were pressed through artificial capillaries developed to hatching (Fig. 1).

To obtain eggs the abdomen of female imagos which showed egg-laying behaviour (for rearing conditions and biology of *Pimpla* see Meng[1]) were torn apart in insect Ringer[6], thereby exposing the ovaries; the eggs were then carefully removed from the ovarioles without pinching. We singled out the eggs which had completed oogenesis, that is eggs which in bright field showed a dark axial column (plasm from the degenerated nutritive chamber[2]) of 60 μm or less measured at 50% of the egg's length. The eggs were transferred into fine watchmaker's oil (Herm. Koch, Hildesheim, No. 1) where most of the adhering Ringer's solution was removed. With the help of a syringe with microfeed equipment (B. Braun, Melsungen) the eggs were then pressed through a polythene capillary. PVC or glass capillaries could not be used, because the eggs stick in them. The problem of getting the eggs through the fine capillaries without splitting the membranes was solved by using the bone oil mentioned above as lubricant (synthetic oils were unsuitable) and also by pressing the wider anterior egg pole first through the narrow passage, instead of the narrower posterior pole as is the case with the ovipositor. The following procedure gave the best results. The egg was pressed little by little into the capillary, until the egg equator reached the narrowest passage. The pressure was then reduced and the egg allowed to slip back. After this the pressure was increased once more until the equator had passed the narrowest passage. Again the pressure was reduced and this time the whole egg slipped slowly through the capillary. For optimum handling of the eggs air bubbles in the oil between egg and pressure site should be avoided. After the treatment the eggs were replaced in Ringer's solution, where the whole of embryonic development took place.

It is not possible to give the exact dimensions of the capillaries we used, because they were irregular. The capillary which proved to be best, however, is shown in Fig. 1*b*; its narrowest passage is 95 μm and its length about 4 mm. In 155 eggs pressed through this capillary fifty-four (34.9%) more or less normal (hatching) larvae and nine (5.8%) abnormal embryos developed.

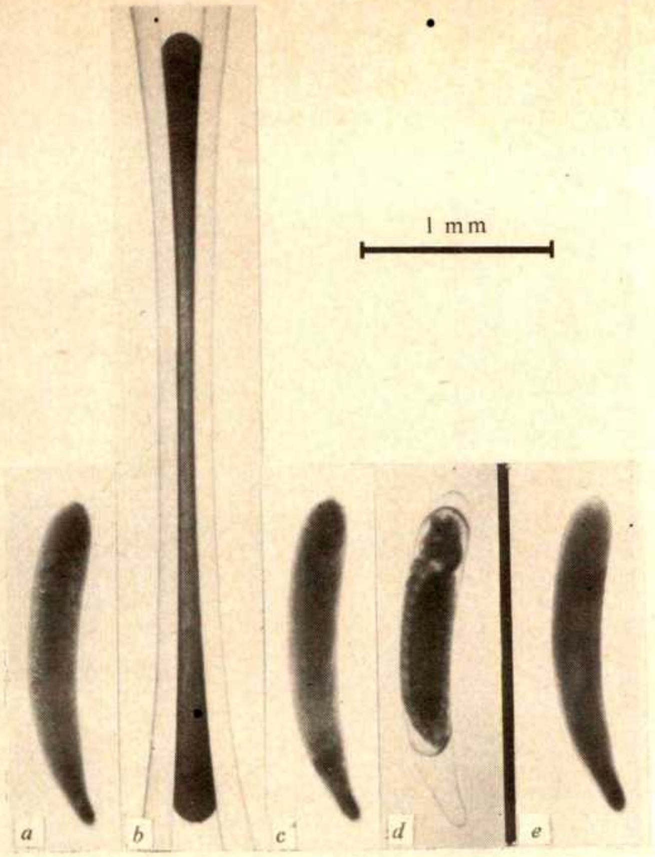

Fig. 1 Unlaid egg before (*a*), during (*b*) and after (*c*, *d*) mechanical treatment and egg after oviposition (*e*). *a*, Egg architecture after explantation from the ovary, in insect Ringer; *b*, egg during mechanical treatment in oil; *c*, egg architecture 4 min after treatment in insect Ringer; *d*, fully-developed embryo 32 h later; *e*, egg explanted from host pupa in insect Ringer 4 min after oviposition, for comparison with *c*. *a*, *c* and *d* show the same egg.

Three of six other capillaries with similar dimensions (smallest passage between 80 and 100 μm; length between 3 and 6.5 mm) tested with five eggs each also produced embryos or larvae (five of fifteen eggs).

Eggs of unmated females (females which had been isolated immediately after hatching) could be activated with the same success as eggs of mated females. Another reason for assuming that all eggs we handled were unfertilized is that the treated eggs had been explanted from the ovarioles and egg insemination in the imago, however, probably takes place in the oviduct or in the vagina. To make certain that these eggs developed males, we implanted forty-one larvae hatching from artificially activated eggs into *Galleria* pupae (method according to Günther[4]). Five imagos hatched, all males. Four of them were tested for fertility by setting them together with two unmated females each. The females put together with two of the males showed that they had been fertilized by producing female progeny. The other two males were presumably also fertile, but the number of offspring tested (five eggs per female) may have been too small.

In the time between explantation of the eggs and their mechanical treatment they could be stored in the Ringer's solution up to 24 h without drastic changes to the egg architecture. They could be induced to start embryogenesis even then, although in a somewhat lower percentage than if immediately after explantation.

According to von Borstel[7,8] who assumed that in the parasitic wasp, *Habrobracon*, egg activation is also achieved by the distortion of the egg during egg laying, the position of the egg nucleus is altered during the oviposition. We can give no information as to a possible displacement of the oocyte nucleus resulting from the egg distortion during oviposition or the mechanical treatment in *Pimpla* as yet, for the nucleus is hard to locate in the egg just before and after the egg is deposited. In any case, the oogenetic architecture of the unlaid egg obviously has to be altered by oviposition such that the induction and coordination of subsequent developmental processes in the egg, like termination of meiosis, intravitelline cleavage and characteristic ooplasm flows, are guaranteed. Whether this also holds true for eggs of other Ichneumonids and perhaps even of other Hymenopteran families is still open for investigation.

No activation of explanted eggs could be obtained by the following methods: temperature shocks, ultrasonic treatment, osmotic shock such as desiccation of the eggs, transferring them into distilled H_2O or hypertonic salt solutions, mechanical treatment other than pressure through capillaries (such as suction through EM apertures or squeezing between glass plates).

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A Carboniferous Insect

AN expedition to search for insects in the Upper Carboniferous freshwater shales of the Hellyer Gorge area of north-western Tasmania in December 1972 was successful. The single specimen obtained is a whole insect (Fig. 1) with wing span of 50 mm, preserving all details of both a fore and a hind wing and some details of the body.

This palaeopterous insect combines characters of the Palaeodictyoptera and Megasecoptera with others unknown in these two orders. The venation is very reduced and closely comparable with that in more generalized megasecopterous wings except that the subcosta ends clearly on the costal margin and slightly beyond the middle of the wing. In contrast to the Megasecoptera, and resembling Palaeodictyoptera, the wings are broad at the base, with the hindwing slightly wider than the forewing.

The body is of simple form, resembling that of Recent stoneflies. Paratergal processes are not present on either the pronotum or segments of the abdomen, as they are in all Palaeodictyoptera and Megasecoptera in which these structures are preserved. The head is slightly longer than wide, and the mouthparts are apparently as long as the head although the structure of this portion of the fossil is confused and possibly includes the basal articles of the antennae. The abdomen appears long due to stretching of the intersegmental membranes during partial break-down of the internal tissues; in life, however, it was probably no longer than the wings.

The palaeoecology of the area of fossilization indicates that the specimen is preserved in the fine sediment deposited at the margins of a small shallow lake adjacent to or in association with glacial moraines. The sediment was almost certainly carried into the lake with the snow-melt. Associated fossils are rare. Plant fronds and pinnules tentatively identified as "*Rhacopteris*" *ovata*, aggregations of a filamentous alga, and an anostracan crustacean have so far been obtained from this series of 1.5 m of shale sediments.

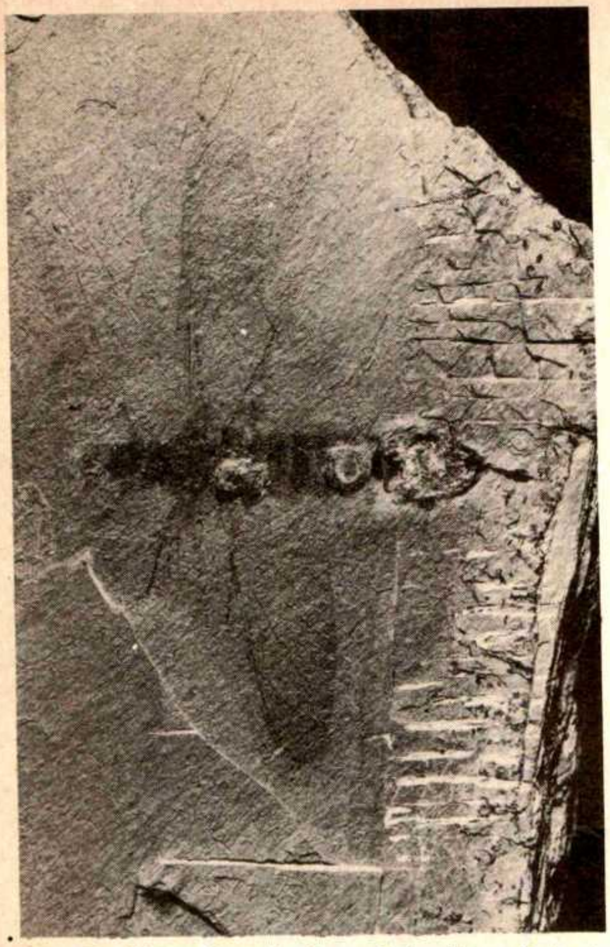

Fig. 1 Fossil insect from the Upper Carboniferous freshwater shales of the Hellyer Gorge in north-western Tasmania.

Abundant animal tracks are preserved in the shale bands of other strata of comparable age in the same area. The shale layers alternate with fine sandstone layers. These tracks of *Tasmanadia twelvetreesi*, described as those of annelid worm[1], and subsequently referred to shrimp-like Crustacea[2], are most probably those of euthycarcinoid Crustacea.

This Upper Carboniferous insect horizon is an outstanding record as not only is it one of the few known Upper Carboniferous horizons, but it is also the known horizon of this age in the southern hemisphere. (An undescribed specimen from the base of the Permian or very top of the Carboniferous has been obtained from a bore core in Rhodesia.) In addition, it lived in ecological conditions much colder than those known for any other Upper Carboniferous insect horizon, which indicates that, even at this early period in their evolution, the insects had adapted to diverse ecological conditions.

The find almost certainly indicates a land connexion between at least Australia and those areas of the northern hemisphere in which insects of comparable or greater age occur, after the origin of winged insects and their occurrence in the Upper Carboniferous of Australia, because not only were insects present in Australia at this time but also because, from the structure of the wings, this type of insect was not adapted to dispersal over long distances.

A more detailed study of the area is planned, in the hope that a more extensive and richer fauna may be found to add to this significant link in the early history of winged insects.

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Potent Pyrethroid Insecticides from Modified Cyclopropane Acids

THE natural pyrethrins[1-3], of which the most important constituent is pyrethrin I (1), are very active against a wide range of insect species, do not leave persistent residues, and have a long record of safe use; despite surprisingly high intravenous toxicity, they have low oral toxicity to mammals[4]. The related synthetic compound, bioresmethrin (2)[5,6], has greater insecticidal activity (for example, about fifty times that of pyrethrin I, by topical application[5], to a normal strain of houseflies), yet is even less toxic to mammals, both orally and intravenously[4,7]. Pyrethrin I and bioresmethrin are esters of (+)-*trans* [1R,3R]-chrysanthemic acid. We have now found that a simple modification of the acid side chain in bioresmethrin by which the four carbon atoms in the isobutenyl group are redisposed to a but-1-enyl substituent (as in 7) produces still greater insecticidal activity (about 100 times that of pyrethrin I to houseflies) whilst retaining low mammalian toxicity. Other changes of the acid side chain in bioresmethrin increase insecticidal activity further; for example the compound (10) with a *cis*-(Z)-butadienyl group and the dichlorovinyl compound (12) are both 2–3 times as potent as bioresmethrin.

In both insects[8] and mammals[9], the *trans* (E)-methyl group (arrow, Fig. 1) of the chrysanthemate side chain in pyrethrin I and related cyclopentenolone esters is a primary centre for metabolic attack. We therefore investigated esters of 5-benzyl-3-furylmethyl alcohol with acids lacking the *trans* (E)-methyl group, hoping thereby to suppress a detoxification route and thus increase insecticidal potency. The ester (4) with a vinyl substituent was less active than the chrysanthemate to houseflies and mustard beetles (Table 1) but the monomethyl compound (5) was more active, particularly to houseflies. Greatest activity in the series to both insects was attained with the but-1-enyl side chain (7), the next two homologues with pent-1-enyl (8) and hex-1-enyl (9) substituents being less toxic.

An even more effective ester (10) (synthesized by the general Wittig route, Fig. 2) had a *cis*-(Z)-butadienyl substituent; this is one of the most potent insecticides known, of any class (LD_{50} 0.002–0.004 μg per insect).

The structures of outstandingly active synthetic pyrethroids (for example compounds (2), (7) and (10) and the ethanochrysanthemate (3)[10], all stereochemically equivalent derivatives of 5-benzyl-3-furylmethyl [1R] 2,2-dimethylcyclopropane carboxylate) thus support the conclusion[7] that an appropriately

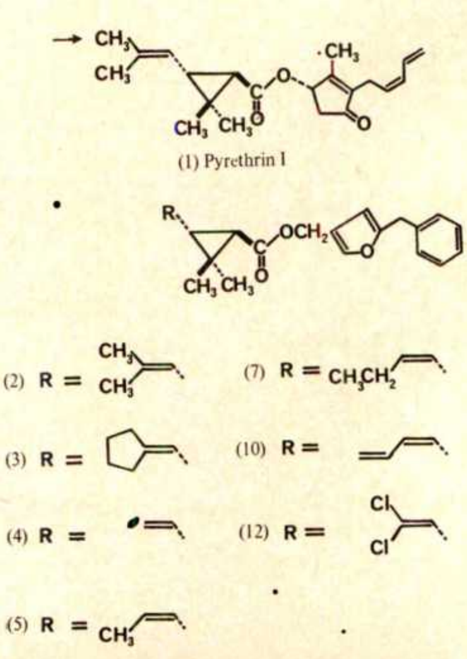

Fig. 1 Pyrethrin I and modifications giving related compounds.

Table 1 Toxicity of Pyrethrin Compounds to Insects and Mammals

		Side-chain (R in second formula)	Relative toxicities* to Houseflies (*Musca domestica* L.)	Relative toxicities* to Mustard beetles (*Phaedon cochleariae* Fab.)	Oral toxicity to rats† (*Rattus rattus*) LD_{50}, mg kg^{-1}
Pyrethrin I	(1)		2	160	260-420 (ref 4)
Bioresmethrin	(2)	2-Methylprop-l-enyl	100‡	100‡	>8,000 (ref 4)
RU 11,679 ["ethanochrysanthemate"]	(3)	Cyclopentylidenemethyl	130	170	100§
	(4)	Vinyl	41	65	
	(5)	Prop-l-enyl (Z)	120	130	>800″
	(6)	Prop-l-enyl (E)	130	130	
	(7)	But-l-enyl (Z)	170	160	800–1,000″
	(8)	Pent-l-enyl (Z)	63	71	
	(9)	Hex-l-enyl (Z)	27	45	
	(10)	Buta-1,3-dienyl (Z)¶	300	300	
	(11)	2-Chlorovinyl	130	130	
	(12)	2,2-Dichlorovinyl	250**	270††	>400″ [(±)-*trans* isomers]
	(13)	2,2-Dichlorovinyl (50/50 mixture of (±)-*cis-trans* isomers)	150	190	40″
	(14)	2,2-Dibromovinyl	110	190	

* By topical application of measured doses in 1 µl of acetone on females (houseflies) or day old adults (mustard beetles) then comparison of LD_{50} values derived from probit analysis.

† Compound administered in glycerol formal (DMSO for compound (1), olive oil for compound (3)).

‡ Taken as standard.

§ Result provided by Roussel-Uclaf.

″ Results communicated by Mr R. D. Verschoyle, Medical Research Council, Toxicology Unit, Carshalton, Surrey.

¶ About 80% Z isomer. The E isomer is less toxic.

** LD_{50} 0.0028 µg/insect (about 0.14 mg kg^{-1}).

†† LD_{50} 0.003 µg/insect (about 0.3 mg kg^{-1}).

orientated gem-dimethylcyclopropane unit is essential for high toxicity to insects. To examine further related compounds we synthesized the monochlorovinyl compound (11) (an isostere of (5)) and, finding it more active than the chrysanthemate (2), made the dichlorovinyl ester (12). The 5-benzyl-3-furylmethyl ester (12) of the (+)-*trans* [1R,3R]-dichlorovinyl acid, obtained by the Wittig route, had exceptional activity, 2–2.5 times as great as that of bioresmethrin. Even the (±)-*cis,trans* form of the acid, synthesized in excellent yield by a development of an earlier process[11], gave an ester with 5-benzyl-3-furylmethylalcohol more active than bioresmethrin, which uses the resolved form, (+)-*trans*-chrysanthemic acid. The ester (14) of the corresponding [1R,3R]-dibromo acid was a little less active, though still very potent.

The compounds described, including the new halogenated derivatives, show that the insecticidal activity of pyrethroids such as bioresmethrin can be increased by small changes in the molecule at sites, such as C-3 on the cyclopropane ring, not directly involved in the poisoning process. The group at C-3 apparently exerts a powerful influence on the level of activity by determining susceptibility to detoxification (*cf.* bioresmethrin[12,13]) and physical properties and so rates of transport into and within the insect. Mammalian toxicity is not influenced correspondingly by the change in structure (see Table 1). The *trans* esters (6), (7) and (12) lack the known specific position of oxidative attack (Fig. 1, arrowed methyl) yet have low oral toxicity to rats, whereas the presence of substituents which sterically hinder esterase action (for example, in the *cis* component of compound (13) and in the tetramethylcyclopropane carboxylates[7]) leads to greater mammalian toxicity. Susceptibility to ester cleavage may thus be more important than attack by oxidases in conferring low mammalian toxicity on pyrethroids (compare ref. 13).

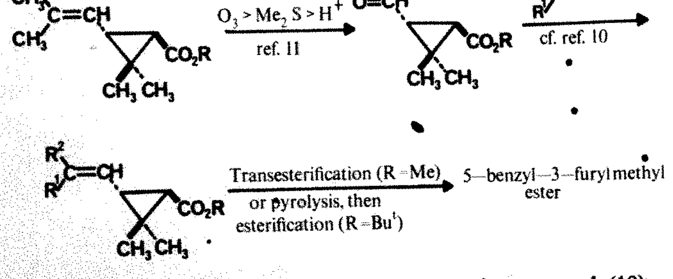

Fig. 2 General Wittig route of synthesis of compound (10).

The new compounds are protected by the UK Patent Applications Nos. 24809/72, 24811/72 and 30838/72. We thank Dr G. Pattenden for generous gifts of methyl (±)-*trans* vinyl and prop-1-enyl2,2-dimethyl-cyclopropane carboxylates[10], used in preliminary work, Dr J. M. Barnes and Mr R. D. Verschoyle for communicating and discussing mammalian toxicity data and the National Research Development Corporation for financial support.

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Experimental Model for Production of Perforating Duodenal Ulcers by Cysteamine in the Rat

It has long been known that exposure to stress, in itself[1] or in combination with various sensitizing agents, particularly glucocorticoids[2,3], can produce acute haemorrhagic erosions of the gastric mucosa which have been used as experimental models of "stress ulcers". However, these erosions have little, if any, tendency to perforate and usually disappear after a few days unless the eliciting stressor is fatal before healing can occur.

On the other hand, rats are unusually resistant to the induction of duodenal ulcers and the few techniques developed for their experimental production are, in general, not readily reproducible because of individual variations in sensitivity and the comparative complexity of the procedures used. Until recently the most rapid and reliable method described was that of Robert *et al.*[4–6], which depends essentially on the continuous subcutaneous infusion of various secretagogues, such as histamine, carbachol and pentagastrin. Yet, to obtain a high incidence, several of these agents must be administered simultaneously during fasting. Another even more complex means for the induction of duodenal ulcers in the rat is the constant perfusion of the stomach and duodenum with acid after introduction of a permanent catheter through a skin incision in fasted and immobilized rats[7].

While studying the effect of hormones on resistance to various toxicants[8], we noted accidentally that acute and almost invariably perforating duodenal ulcers developed in rats given cysteamine-HCl (β-mercaptoethylamine-HCl) either orally or parenterally. Essentially similar results were obtained in the course of these same studies in rats treated with 3,4-toluenediamine[9] or propionitrile[10], but the ulcerogenic effect of cysteamine is even more rapid and constant, thus providing a particularly reliable model for investigations on the mechanism of duodenal ulcerogenesis and possible means for its prevention.

All our experiments were performed on female Sprague-Dawley rats (Canadian Breeding Farms) with an average initial body weight of 100 g (range 90–110 g). Throughout the period of observation, the animals had free access to Purina Laboratory Chow and tap water.

Cysteamine-HCl (given by the California Foundation for Biochemical Research) was administered at the dose of 100 mg in 1 ml water orally once, or 50 mg in 0.5 ml water subcutaneously once, on the first day to two groups of ten rats each. Preliminary experiments had shown that smaller amounts do not consistently produce duodenal ulcers and similar doses of cysteamine are fatal within minutes or hours when given intravenously or intraperitoneally, and so unsuitable for our purpose.

It is important to emphasize, however, that in the group receiving a single oral dose of 100 mg of cysteamine, mortality within the first 48 h was 70%, and all animals had grossly evident duodenal ulcers. In general, the lesions began with the formation of an oval reddish spot about 3×5 mm in size just below the pylorus. Subsequently, this entire region became liquefied and the pyloric contents escaped into the peritoneum (Fig. 1). Yet generalized peritonitis was sometimes avoided through the formation of adhesions between the pylorus and the liver. In these instances, a deep cavity developed in the adjacent hepatic parenchyma as a consequence of erosion by the duodenal digestive juices.

Subcutaneous administration of cysteamine was less consistently effective in producing duodenal ulcers. This is probably due to the fact that 100 mg of the compound, given subcutaneously, caused immediate mortality in most cases, and so we had to limit the dose to 50 mg once subcutaneously on the back. Under these conditions, seven out of ten animals died within 48 h and five of these exhibited perforating duodenal ulcers. Consequently, as a routine model for the production of these lesions, only oral administration can be recommended, but it is of theoretical importance to know that the compound does not act merely by direct contact with the duodenum.

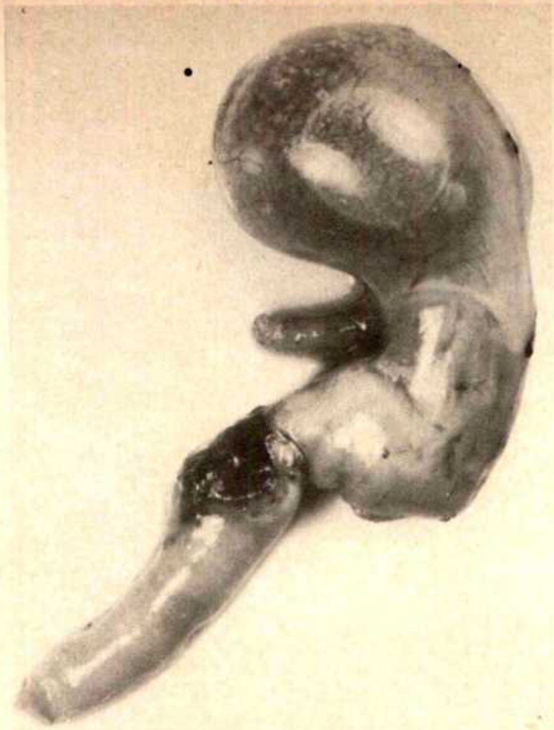

Fig. 1 Gross appearance of a perforating duodenal ulcer just distal from the pylorus. The affected region is haemorrhagic and liquefied.

It is evident that cysteamine given orally or parenterally is highly active in producing circumscribed and usually perforating duodenal ulcers in rats. This effect is obtained in animals allowed free motion with access to food and water during the entire period of observation. In the course of our systematic studies on the effects of hormones and nonhormonal microsomal drug-metabolizing enzyme inducers on the toxicity of various agents, we have noted the occasional occurrence of duodenal ulcers after poisoning with acetanilide, allylchloride, acetaminophen or 4,4-diaminodiphenylmethane. However, among the compounds tested so far, only propionitrile and 3,4-toluenediamine induced a very high incidence of perforating duodenal ulcers within a few days following oral or parenteral administration[9,10].

None of these substances is as reliable as cysteamine in regularly producing perforating duodenal ulcers after a single oral dose, but the fact that so many compounds, widely differing in chemical structure and pharmacological properties, have such a selectively destructive effect on the same segment of the duodenum is noteworthy and will be investigated further. In man, "stress ulcers" are frequently localized in the duodenum but in the rat this is quite exceptional and multiple gastric erosions are the most characteristic gastrointestinal manifestations of exposure to stress. The ability to elicit circumscribed duodenal ulcers in rats is not merely a nonspecific stress effect but, in view of the many agents capable of inducing such lesions, some relation to nonspecific stress may be suspected. Possibly, certain chemical characteristics of the toxicants require "conditioning" by stress factors in order to acquire toxicity for the tissues of this particular region.

As cysteamine was used for experimental purposes by many investigators, it is somewhat unexpected that this particular effect on the duodenum appears to have escaped attention.

In the course of a study on osteolathyrism, Lalich[11] noted that if large amounts of cysteamine were mixed with the diet of rats, they caused loss of weight and "minimal osteolathyrism". Yet no mention was made of any intestinal lesions.

Special attention was given to cysteamine and related compounds because of their radioprotective effect[12–18]; although in many of these studies sublethal and even lethal amounts were used, we could find no description of any duodenal lesions.

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Symbiosis between *Rhizobium* and the Non-legume, *Trema aspera*

ROOTS of *Trema aspera* Decaisne plants growing between rows of tea in the Pangia District of New Guinea showed abundant nodulation, similar to the nodules found on many tropical legumes. Non-flowering nodulated plant specimens were identified by the botanists of the Department of Forests, Lae, New Guinea.

Trema aspera belongs to the family Ulmaceae. Reviews[1–6] of non-legume plants bearing nodules do not record root nodules on plants in this family. Attempts to isolate and identify the endophytes from these known non-legume nodules have been summarized[3,6] and indicate that the endophyte has marked affinities with the actinomycetes. Nodulation has been recorded[7,8] on a further seven plant species of non-legumes in five plant families. "*Rhizobium*-like" organisms have been isolated[8] from nodules formed on *Artemisia ludoviciana* (Compositae) but the isolates in pure culture were unable to form nodules on plants in their laboratory.

Root nodules (5–10 mm long by 1–1.5 mm diameter) from *T. aspera* were collected on two occasions and culture of the endophyte attempted. Only one type of microorganism grew on yeast-mannitol agar plates inoculated from six nodule squashes on each occasion. The abundant growth indicated that these organisms were present in large numbers. Nodule squashes examined by phase contrast microscopy showed rods resembling the bacteroids of *Rhizobium* in nodules from *Vigna sinensis* and other tropical legumes.

In laboratory culture, the isolated bacteria (strain NGR 231) are rods, mainly straight but sometimes curved, occurring singly, with two refractile areas near the ends of the cells. Cultures heated at 75° C for 30 min failed to grow, indicating that the *Trema* isolates do not contain spores. The bacterium is motile, Gram negative, and measures 1.7–3.5 μm × 0.7–0.9 μm. Electron micrographs of young cultures show subpolar flagellation of the bacterium. After 10 d incubation, the colonies produced are circular, 1 mm in diameter, and convex in elevation; the surface is smooth and glistening; it is opaque and white but may develop a brown pigment with age. Cultures utilize dextrin, inulin, maltose, fructose, galactose, glucose, mannose and rhamnose but the preferred carbon sources are arabinose and xylose. Growth in litmus milk results in an alkaline reaction with the formation of a narrow serum zone. These features are typical of slow-growing strains of *Rhizobium* sp.

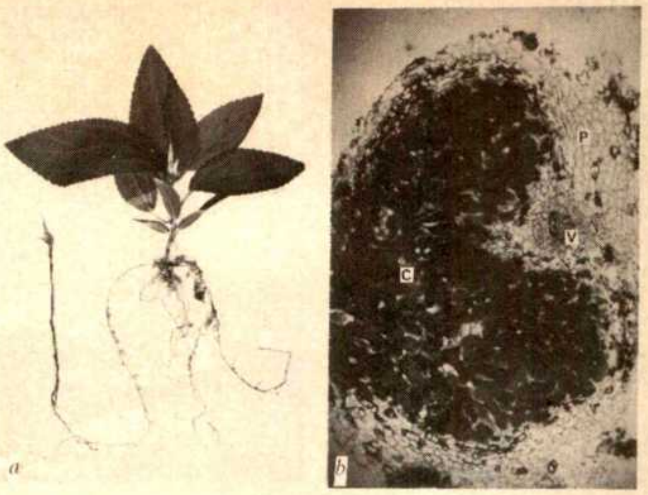

Fig. 1 *a*, Nodulated *Trema* plant. *b*, Internal structure of nodule developed on *Trema* following inoculation with strain NGR 231 (×32) showing cortical parenchyma cells (P), vascular bundles (V) and innermost bacteroid area (C).

Strain NGR 231 was tested for its ability to nodulate *T. aspera* (seed supplied by the Department of Agriculture, Stock and Fisheries, New Guinea, from the Tambul District, 80 km from Pangia) and a number of legumes representing the main cross inoculation groups. All species were grown in Leonard jar assemblies[9], either uninoculated (with and without adequate combined nitrogen) or inoculated with strain NGR 231. In addition, the legumes were inoculated with known effective strains of *Rhizobium*. All treatments were in triplicate, with two plants per assembly.

Trema formed nodules in response to inoculation with strain NGR 231. The nodules were effective in nitrogen fixation, as shown by the strong growth of nodulated plants (Fig. 1*a*) in a rooting medium devoid of combined nitrogen. Acetylene reduction assays for nitrogenase activity[10,11] gave positive results with nodulated whole plants and detached nodules, but not with roots without nodules (Table 1) indicating that N_2 fixation was restricted to the nodule. The low value for detached nodules parallels the diminished activity of detached legume nodules[11,12]. The mature nodules were often 7 mm in length, loosely attached to the root and were elongate with branching (see ref. 13).

Table 1 Acetylene Reduction Assay of *Trema aspera* Nodules and Root Tissue Following Inoculation with Strain NGR 231

Material assayed	μmol C_2H_4 g^{-1} nodule fresh wt h^{-1}
Nodulated plant 1	11.5
Nodulated plant 2	11.7
Detached nodules (6)	4.6
Nodule-free roots (2)	0

All uninoculated legume plants were free of nodules while effective nodulation with strain NGR 231 was obtained on plants of four species (*Vigna sinensis*, *V. sinensis* ssp. *sesquipedalis*, *Macroptilium atropurpureum* (formerly *Phaseolus* *atropurpureus*), and *M. lathyroides* (formerly *P. lathyroides*)). The nodules were pink, large, and typical of the nodules produced by effective "cowpea-type" rhizobia[13]. The fifteen species which failed to nodule included *Lablab pupureum* (formerly *Dolichos lablab*), *Crotalaria anagyroides, Glycine max, Acacia farnesiana, Phaseolus vulgaris, Trifolium pratense,* and *Medicago sativa.*

Haematoxylin stained sections of NGR 231 nodules formed on the four legumes were structurally similar to the nodules produced by authentic *Rhizobium* strains on these species. The structure of the nodules formed on *Trema* resembled the overall histological pattern of legume nodules, and thus was quite unlike that of non-legume nodules such as those of Alder. Cortical parenchyma cells, a peripheral vascular system and an innermost bacteroid area consisting of plant cells packed with bacteria, are shown in Fig. 1*b*.

Cultures isolated, and bacteroids, from nodules on glasshouse grown plants of *Trema* and legumes were specifically agglutinated by the antiserum for NGR 231. The specific reaction only occurred after the antigen was heated at 100° C for 1 min[14]. The serological specificity of NGR 231 antiserum was demonstrated by its failure to agglutinate any of forty-three *Rhizobium* strains originating from nodulated legumes grown in New Guinea and representing a number of cross inoculation groups.

The probable phylogeny and relationships of the Orders of Angiosperms, as given by Hutchinson[15], place the Urticales (of which the family Ulmaceae is a member) in the same evolutionary line as other nodule bearing Orders. My results show that *Trema aspera* may now be added to the list of nitrogen fixing nodulated plants, that the endophyte is a bacterium (which is of interest in that most endophytes of non-legume nodules have so far defied isolation and precise identification) and that the bacteria satisfied the criteria necessary to classify them as *Rhizobium* species. The *Trema* root nodule bacterium is the first of the rhizobia known to effectively nodulate a non-legume.

The initial observations, the isolation of the endophyte and preliminary inoculation trials were done whilst I was an officer of the Department of Agriculture, Stock and Fisheries in New Guinea.

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Isolation of Legume Root Nodule Protoplasts

INTEREST has developed in the use of cultured cells for establishing symbiosis between *Rhizobium* and plant cells *in vitro*[1], and in the genes controlling nodulation and the regulation of nitrogen fixation[2]. It has, however, been impossible to isolate single cells from infected nodules. Such infected nodule cells would be particularly useful for biochemical studies on nitrogen fixation of infected cells *in vitro*. Recent studies on the somatic hybridization of plants by the fusion of isolated protoplasts suggest that hybridization between legumes and non-legumes may afford a means of transferring the genetic capability of symbiotic nitrogen fixation from legumes to non-legumes[3]. Protoplasts can be readily isolated from leaves and many other plant tissues using cell wall degrading enzymes, and these naked single cells can often be readily cultured *in vitro*[4]. We have therefore investigated the possibility of isolating protoplasts from legume root nodules.

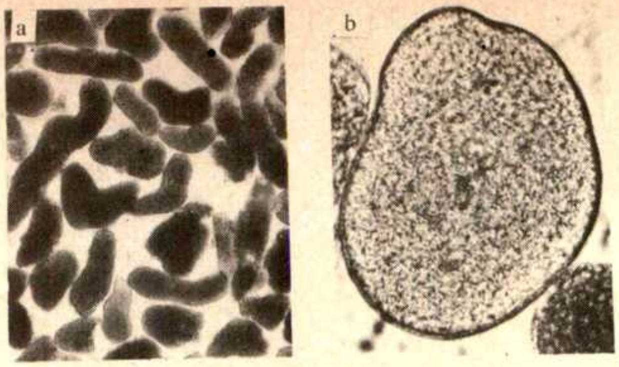

Fig. 1 *a*, Freshly isolated soybean root nodule protoplasts. Light micrograph ×20. *b*, Single root nodule protoplast. Bacteroids in the cytoplasm give the protoplast a granular appearance. Light micrograph ×80.

The seeds and seedlings of soybean (*Glycine max* var Grant) were inoculated with *Rhizobium leguminosarum* (Rothamsted Culture Collection No. 3407). Bacteria for inoculation were cultured as previously described[5]. Young root nodules 4–8 mm in diameter were selected from 16–24 week old plants, surface sterilized in 10% v/v 'Domestos' (Lever Bros. Ltd) with 0.5% v/v 'Teepol' (BDH Chemicals Ltd) for 20 min, and washed with eight changes of sterile water. Nodules (1 g fresh weight) were cut into slices (~ 0.3 mm thick) and incubated in 10 ml of a 'Millipore'-filtered enzyme mixture of 1.5% 'Cellulase' R10, 0.5% 'Macerozyme' R10 (Kinki Yakult Manufacturing Co. Ltd, Nishinomiya, Japan) with 1.0% 'Rhozyme' HP 150 (Rhom and Hass Co. Ltd, Philadelphia) in 0.65 M mannitol (*p*H 5.8) for 5 h at 20° C in the dark with gentle agitation on a horizontal shaker (70 r.p.m.). The material was then teased apart and incubated without shaking for 1 h. The protoplast-enzyme mixture was strained through a fine wire gauze to remove debris. Protoplasts were allowed to settle, the supernatant removed, and the protoplasts washed with six changes of 0.65 M mannitol. Protoplasts were fixed for electron microscopy in 3% glutaraldehyde in 0.1 M sodium phosphate buffer (*p*H 7.0) containing 0.65 M mannitol for 16 h at 22° C. Further stages of preparation were as already described[5].

Almost complete digestion of the pink-infected nodule tissue occurs using the enzyme mixture described, and 0.6–1.0 × 10⁶ protoplasts per g fresh weight of nodule material are freed. Protoplasts are also liberated using only 'Cellulase' with 'Macerozyme', but tissue maceration and protoplast release are stimulated by the addition of 'Rhozyme'. Most protoplasts were elongated (Fig. 1*a*) and usually retained the shape of the infected cells in the nodule tissue. Failure to become spherical probably results from the large number of bacteroid-containing vesicles in the cytoplasm (Figs 1*b*, 2*a*, *b*) and the absence of a large central vacuole. Thin sections examined electron microscopically showed no cell wall material present at the plasmalemma surface (Fig. 2*b*). 50–60% of the soybean nodule protoplasts appeared viable on isolation as judged from their ultrastructural appearance and fluorescence when viewed optically using fluorescein diacetate[6]. When the plasmolyticum was reduced to 0.5 M mannitol the protoplasts burst releasing free bacteroids and also vesicles containing bacteroids (Fig. 2*c*).

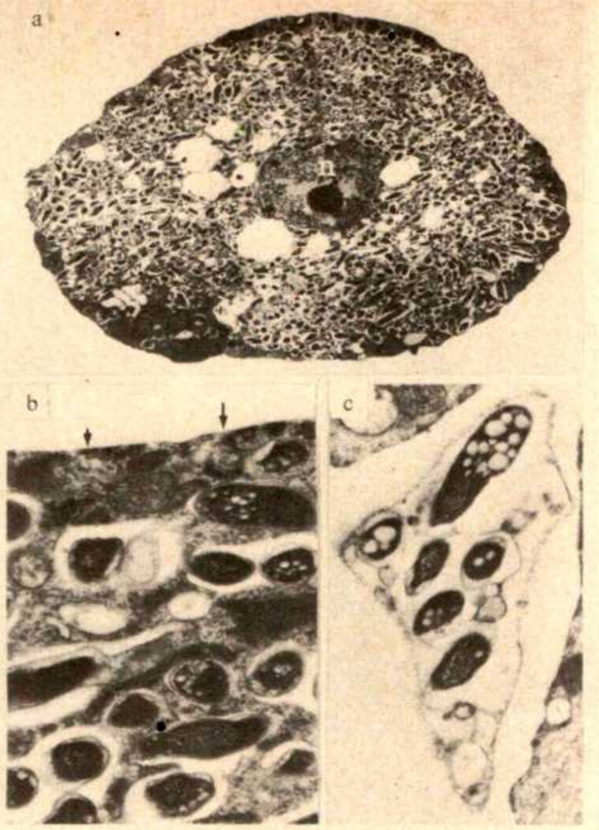

Fig. 2 *a*, Low magnification electron micrograph of a root nodule protoplast. Many bacteroid-containing vesicles are present in the cytoplasm. Nucleus with nucleolus (n). ×1,500. *b*, Electron micrograph of the peripheral region of an isolated root nodule protoplast. The plasmalemma (arrowed) is free of cell wall material. Bacteroids are present in vesicles in the cytoplasm. ×15,000. *c*, Electron micrograph of a membrane-bounded vesicle, enclosing bacteroids, released from a burst root nodule protoplast. ×11,000.

Protoplasts have also been isolated using this procedure from young root nodules of lupin (*Lupinus polyphyllus hybrida*).

As already indicated, these isolated root nodule protoplasts should be particularly useful for biochemical and somatic hybridization studies in connexion with nitrogen fixation. Moreover, vesicles containing bacteroids, which have been suggested as "nitrogen fixing units"[7], and which have been seen to be released from burst nodule protoplasts, may also be of use in these studies.

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Effect of Dibutyryl Cyclic AMP and Other Nucleotides on Nitrogen Fixation by Legume Root Nodules

CYCLIC AMP mediates reactions in tissues of animals, plants and microorganisms (for reviews see refs 1 and 2). Here we report that dibutyryl cyclic AMP inhibits the fixation of atmospheric nitrogen by nodules of three legumes, *Trifolium repens*, L. (white clover), *Medicago sativa*, L. (alfalfa or lucerne) and *Lotus pedunculatus*, Cav. (lotus). On the other hand, we have found that free cyclic AMP and AMP enhance nitrogen fixation by these nodules.

The rate of acetylene reduction was used as a measure of nitrogen fixation because of its high sensitivity and because data indicate that it correlates closely with nitrogen fixation[3,4]. Plants were grown from surface-sterilized seed placed singly under sterile conditions in test tubes containing 10 ml of agar medium[5]. The tubes were kept in a glasshouse where light was equally distributed. Ten days later the seedlings were inoculated with the appropriate strain of *Rhizobium* sp. suspended in 1 ml of water. When nucleotides were used the rhizobia were suspended in 1 ml of a solution containing 10 μmol of nucleotide in most experiments. Seven weeks after inoculation the rate of acetylene reduction was determined[4,6]. Each result was assessed from the average of those for ten studies.

Table 1 Effect of Dibutyryl Cyclic AMP and AMP on the Rate of Acetylene Reduction by Legume Nodules

	Rate of acetylene reduction nmol per plant h^{-1}		
Legume	Control	+ Dibutyryl cyclic AMP	+AMP
Clover	15.6	1.1	31.2
Lotus	11.3	2.0	33.5
Alfalfa (lucerne)	21.6	0	29.7

The results in Table 1 show the effect of dibutyryl cyclic AMP and AMP on the rate of acetylene reduction by nodules formed by each of the three legumes. Although the plants treated with dibutyryl cyclic AMP formed nodules, the rate of acetylene reduction by these nodules ranged from an unmeasurable level in alfalfa to 19% of that of the control in lotus. The rate of acetylene reduction by nodules on plants treated with AMP was 30–200% greater than that observed in control plants.

The decrease of the rate of nitrogen fixation in the presence of dibutyryl cyclic AMP could be due to the action of the nucleotide on (1) the host plant, (2) the growth of rhizobia or (3) the process of invasion by rhizobia of the host cells and the subsequent transformation of the non-nitrogen fixing rhizobia to the nitrogen fixing bacteroids in the host cells. Experiments were therefore carried out with white clover to study the effect of dibutyryl cyclic AMP on the growth of plants supplied with potassium nitrate and therefore not dependent for their nitrogen supply on symbiotic fixation of atmospheric nitrogen. These experiments were also planned to compare the effect of dibutyryl cyclic AMP with that of free cyclic AMP, AMP and guanosine monophosphate (GMP) on growth and nitrogen fixation.

When dibutyryl cyclic AMP was present the rate of growth of plants (expressed as fresh weight) which depended for their nitrogen on symbiotic nitrogen fixation decreased in proportion to the concentration of the nucleotide. On the other hand, the rates of growth of plants grown in media containing potassium nitrate were not affected by dibutyryl cyclic AMP (Fig. 1 and Table 2). These results indicate that the inhibition of growth by dibutyryl cyclic AMP was not due to an effect on the host plant when the plant was not dependent on fixation of atmospheric nitrogen.

Dibutyryl cyclic AMP decreased the rate of nitrogen fixation and plant growth whereas free cyclic AMP, AMP or potassium nitrate (nitrogen equivalent to that in 10 μmol AMP used)

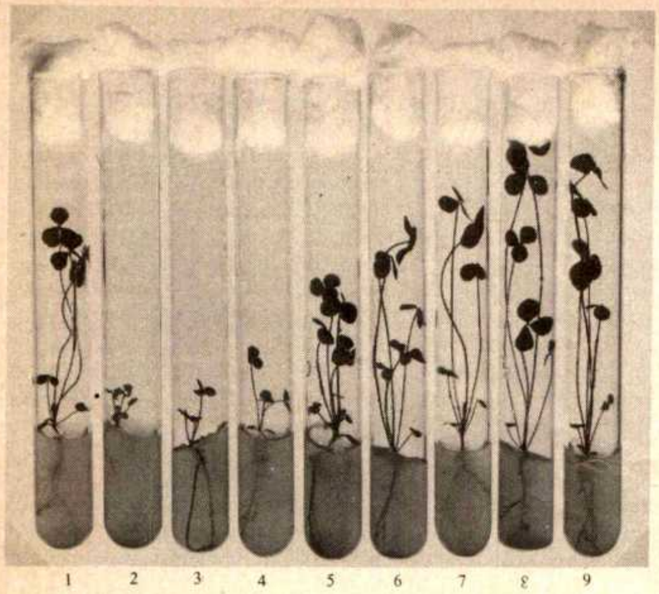

Fig. 1 1, Control; 2, +dibutyryl cyclic AMP (10 µmol per tube); 3, +dibutyryl cyclic AMP (5 µmol per tube); 4, +dibutyryl cyclic AMP (2.5 µmol per tube); 5, +potassium nitrate+dibutyryl cyclic AMP (10 µmol per tube); 6, +potassium nitrate alone; 7, +cyclic AMP; 8, +AMP; 9, +GMP.

increased the rate of nitrogen fixation and plant growth. The enhancement of growth and nitrogen fixation by free cyclic AMP, an opposite effect to that observed with the dibutyryl derivative, may be due to the rapid breakdown of free cyclic AMP by the phosphodiesterase. The product of this degradation, AMP, increased nitrogen fixation and plant growth (Tables 1 and 2). It has been reported[7] that bromoderivatives of cyclic AMP are far more resistant than free cyclic AMP to degradation by plant phosphodiesterase.

Table 2 Effect of Dibutyryl Cyclic AMP, Cyclic AMP, AMP and GMP on Rates of Growth and Acetylene Reduction by White Clover Nodules

Treatment	Rate of acetylene reduction nmol per plant h^{-1}	Average fresh weight of plant (mg)
Control	16.6	90
+dibutyryl cyclic AMP (10 µmol per tube)	1.1	10
+dibutyryl cyclic AMP (5 µmol per tube)	1.9	20
+dibutyryl cyclic AMP (2.5 µmol per tube)	4.7	30
+cyclic AMP (10 µmol per tube)	20.8	130
+AMP (10 µmol per tube)	31.2	190
+GMP (10 µmol per tube)	16.2	180
+N (equivalent to amount in 10 µmol AMP) added in the form of potassium nitrate	26.6	210
+N_2 (equivalent to amount in 10 µmol AMP)+dibutyryl cyclic AMP (10 µmol per tube)	0	190

The increase in the rate of nitrogen fixation by AMP may be due to either a specific effect of this nucleotide on nitrogen fixation or the supply of minute amounts of nitrogen which had been shown to increase the rate of nitrogen fixation in several legumes (unpublished data of A. H.). This was confirmed in the work described here by the increase in nitrogen fixation in the presence of potassium nitrate containing an equivalent amount of nitrogen to that in AMP used (Table 2). Guanosine monophosphate (GMP), unlike AMP or free cyclic AMP, had no effect on nitrogen fixation but it increased the rate of plant growth (Fig. 1 and Table 2). This is difficult to explain by the data presented here.

Preliminary experiments to study the effect of dibutyryl cyclic AMP on the growth of the rhizobial strains used in this work showed that this nucleotide did not reduce the rate of growth of these bacteria when cultured on yeast mannitol agar media[8].

The results of this work thus showed that dibutyryl cyclic AMP reduced the rate of nitrogen fixation by legume root nodules and that this effect was not exerted by affecting the growth of the host plants or rhizobia when either were grown independently. The effect of dibutyryl cyclic AMP may be at the level of transformation of rhizobial cells into nitrogen fixing bacteroids after invasion by the bacteria of the host plant root cells.

The amounts of cyclic AMP and dibutyryl cyclic AMP used in this work are 10–100 times the normal physiological range, but the amounts of these nucleotides transported across membranes of rhizobial and plant cells remain to be determined.

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Epidemic Spread of a Rust imported for Biological Control

IN 1971 the autoecious rust fungus *Puccinia chondrillina* Bubak and Syd. was imported into Australia from Europe, an important step in the programme for the biological control of skeleton weed *Chondrilla juncea* L., an extremely serious weed of cultivation in south-east Australia[1]. This followed three years of intensive testing and discussion[2,3], and represented a highly significant event in Australian quarantine policy. We believe that this is the first example in the recent history of quarantine controls, of the deliberate introduction and successful release in a new country of a plant pathogen for weed control.

The strain introduced was selected on the basis of its virulence against the form of *C. juncea* (an apomict) widespread in Australia and was isolated from a form of this species in Italy seemingly identical with the common Australian form. Following satisfactory demonstration of specificity, this strain was established in quarantine in Canberra and was released in mid 1971 after screening.

Figure 1 shows the distribution of *C. juncea* in Australia and the location of release sites. Where distribution is practically continuous, densities in disturbed land often exceed 100 plants m^{-2}. The sites are representative of the different environments colonized by the weed and, at several, work had already been carried out on the population dynamics of *C. juncea*[4]. The climate ranges from dry, predominantly winter rainfall regions in the west (some with irrigation) through a region of increasing rainfall to predominantly summer rainfall areas in the north. Field infections were established at all sites at different times from June to December 1971, but the first successful field infection in Australia was made at Wagga.

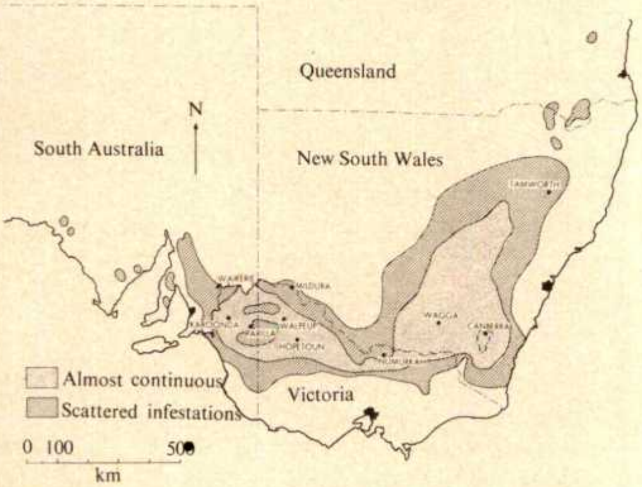

Fig. 1 The present distribution of skeleton weed *Chondrilla juncea* L. in Australia.

On June 10, 1971, nine plants infected with *P. chondrillina* (100–200 uredosori each) were transplanted into the centre of a 0.1 ha plot containing a dense growth of *C. juncea* (143 ± 19 rosettes m^{-2}). Subsequent events are related to an approximate time scale in generations based on the known relationship between minimum generation time and temperature[5], combined with air temperature records for Wagga.

At slightly over one generation time a few uredosori (about 50 total) were observed on plants close to the transplants. Most were within 20 cm but one was found 1 m distant. With additional infections by spores from the transplants the intensity of this initial secondary infection had increased markedly when inspected just before the completion of the second generation. When this plot was next examined, in early November, after the fifth completed generation, it was apparent that conditions had been favourable for the pathogen. The majority of plants in the plot were infected, some severely (500–2,000 uredosori per plant), and uredosori were found up to 27 m from the centre of the plot. This focus, though still well defined, was obviously large enough to produce infections some distance away.

Two generations later, stands of *C. juncea* were searched 8, 16 and 24 km distant in different directions. Foci could be found in all stands examined at 8 km and at two foci the infection was estimated to be in its third generation. At 16 and 24 km foci were found in 50% of the areas searched, each focus being judged to be two generations old. It was therefore apparent that infections had been started at least 8 km away, four generations after the original transplants were introduced and, similarly, at least 24 km away after five generations. This initial stage of development seems to have been on a scale only slightly less than that recorded for wheat stem rust epidemics[6,7].

The spread continued to be rapid thereafter, and it was possible to trace the course of the epidemic with the aid of individual sightings, questionnaires and field surveys.

Foci at minimum distances of 80 km, 160 km and 320 km were probably initiated at the eighth, tenth and twelfth generations approximately, after the initial introduction at Wagga. One hundred kilometres to the east and 320 km to the north would probably have been the limits of independent spread, the distribution thereafter overlapping those spreading from Canberra and Tamworth where initial infections were established later. By late March 1972 there was only one undoubted negative record in all stands of *C. juncea* examined in New South Wales, including one of the northerly isolated areas.

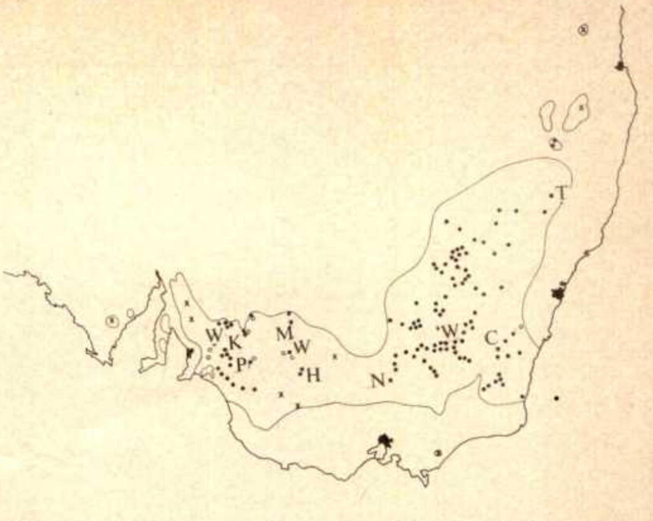

Fig. 2 Distribution of positive and negative records of *Puccinia chondrillina* as at March 31, 1972. ●, Positive identification by March 31; ○, confirmed negative record at March 31; ×, later positive identification (only significant records shown).

In the southern and western region of *C. juncea* distribution, the drier summer produced a different situation. Following initial establishment of foci at considerable distances from some sites, spread was curtailed. Surveys in March 1972 showed an irregular pattern of presence and absence which contrasted with the general distribution in New South Wales (Fig. 2). Following autumn rains in March and April, however, further surveys indicated a general distribution here also.

It was not possible to examine the small isolated areas of *C. juncea* well outside of and to the north, south and west of the main range until varying intervals later, but all were known to be colonized by *P. chondrillina* by December 1972 at latest.

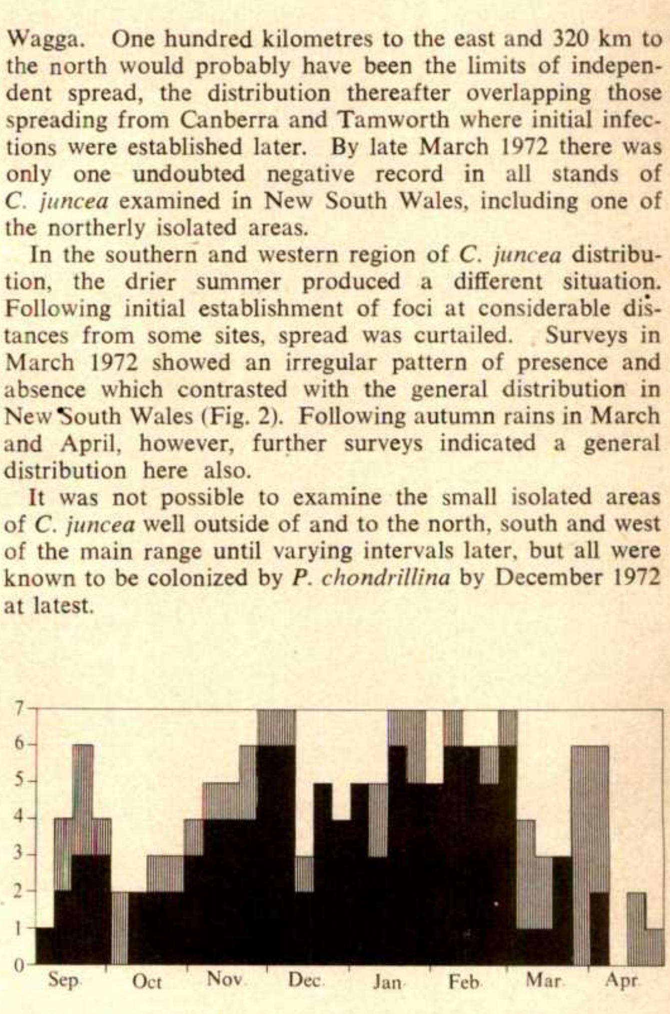

Fig. 3 The number of nights per week when infection by *P. chondrillina* was successful in the field. 1971–1972. ■, Massive infection; ▥, at least some infection.

In New South Wales, above-average rainfall made the summer suitable for fungal infection. A daily survey of the suitability of meteorological conditions for infection has been carried out at Canberra using spore-dusted plants exposed for 24 h periods in the field, and the results of this bioassay for the period of major spread are shown in Fig. 3.

Apart from lower overnight temperatures in spring, Canberra experienced rainfall and temperature conditions very similar to those of Wagga 150 km away. Winds were predominantly easterly but there were also significant northerly and south-westerly currents.

The plant disease epidemic seen on this occasion has the unique double distinction of being observed on a grand scale and of being both deliberate and beneficial. The density of the host, the virulence of the pathogen and the weather conditions together ensured its success. It is of historic interest that the major spread was from Wagga which was the centre of dispersal of the host *C. juncea*[8] 60 yr earlier.

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Filaments but no Membranous Transcellular Strands in Sieve Pores in Freeze-etched, Translocating Phloem

PLANT physiologists agree that organic substances are transported long distances in plants through sieve-tube elements and through pores in the sieve plates between them. But they disagree about how this transport is driven; sieve tubes might be passive pipes between source and sink or might contain pumps all the way along. This controversy drags on because microscopists suspect that the contents of sieve elements may be altered or displaced as they are prepared for microscopy; thus their *in vivo* configuration remains uncertain. No electron micrograph has yet been published of a sieve element confirmed as translocating when it was fixed.

The outstanding question has been "What is in pores in sieve plates between translocating sieve elements?"[1–4]. In the electron microscope sieve pores often appear to contain closely packed filaments ("p-protein"). Weatherley[5] has calculated that if these are normally closer than 1000 Å then their resistance to flow will be so high that Münch's simple pressure-flow hypothesis is not adequate to account entirely for translocation; pumps would be needed at places along sieve tubes. Furthermore, he calculated[5] that the pressure-flow hypothesis might be feasible if filaments in the lumen of sieve elements are bundled together but that if they are uniformly dispersed it would require a pressure gradient larger than that available in the plant. Thus we need also to know whether filaments in the lumen of translocating sieve elements are dispersed or arranged in separate bundles.

Thaine and his co-workers[6,7] concluded from light microscopy that "transcellular strands of cytoplasm" lie through sieve pores and provide pathways for translocation. In an earlier paper[8] Thaine stated that, theoretically, such transcellular strands should be enclosed by a membrane which he believed "to have structural and physiological properties comparable with the tonoplast". More recently he has speculated on the probability of transcellular strands with a contractile structural boundary formed from one or more rings of protein filaments which enclose endoplasmic tubules and perhaps spherosomes and plastids[9]. He speculates that endoplasmic tubules, each about 1 μm wide, might occupy about 70% of the area of cross section of each strand and might be connected to the endoplasmic reticulum along the side walls and at the ends of sieve tubes. He suggests that such hypothetical transcellular strands could drive translocation by peristalsis.

Arguments for true membranes around transcellular strands in sieve elements have come from light microscopy and from analogy with transvacuolar strands in other kinds of cells[8]. But the light microscope does not resolve membranes in cells and cannot, therefore, be used to identify them with certainty in sieve elements. Membranes have never been demonstrated around or within elaborate transcellular strands in sieve elements as proposed by Thaine[9]. At most, some narrow cisternae of endoplasmic reticulum have been shown in sieve pores in some plants[10–12]. Thaine[9] suggests that his membranous transcellular strands fail to appear in the electron microscope because they are degraded by the methods commonly used to fix, dehydrate, or embed them.

Jarvis and Thaine[7] thought that "progress might be made if sieve tubes were fixed rapidly by freezing rather than by chemical means". They froze intact vascular bundles rapidly, sectioned them in a cryostat, thawed the sections rapidly, and examined them in 1% glutaraldehyde under the light microscope. They show clear photographs of stainable strands, 5–9 μm wide in a sieve element, and interpret them to have a "discrete boundary enclosing groups of parallel substructures".

Previously, Johnson[3] had found filaments but no sign of membranous strands in sieve pores in vascular bundles which were frozen rapidly while intact between leaf and plant and then freeze-etched for electron microscopy. The vascular bundles freeze-etched by Johnson[3] or those sectioned and fixed by Jarvis and Thaine[7] might not, however, have been translocating before they were frozen.

Here, I describe electron microscopy of freeze-etched sieve elements and sieve pores in vascular bundles which were translocating ^{14}C. These bundles were frozen intact to below −50° C in less than 0.03 s.

Whole plants of *Nymphoides peltata* (S. G. Gmel.) O. Kuntze, a water plant with floating leaves, were arranged with their long petioles extended across a flat platform. The leaves were illuminated in separately transparent chambers. Epidermis and aerenchyma were dissected from each petiole from about 6 cm to 11 cm below the leaf leaving the central vascular bundle only. More than 1 h after dissection $^{14}CO_2$ was applied to the leaves for 10 min. The petioles were left for a further hour to translocate, and the exposed vascular bundle of each petiole was then gently but rapidly immersed in liquid Freon 22 at about −145° C. The frozen segment was broken from the plant and transferred to liquid nitrogen. Samples of petiole below it were measured for radioactivity with a Packard Tricarb liquid scintillation spectrometer. Only those pieces of frozen vascular bundle which proved to have translocated normally were used. They were stuck to gold disks whilst still below −70° C and freeze-etched as described by Johnson[3]. No fixatives or cryoprotective substances were used.

The time taken for ^{14}C to reach the youngest leaves showed that transport velocity can exceed 40 cm h^{-1}.

Figure 1 shows part of a freeze-etched sieve plate between two mature sieve elements, and part of an adjacent parenchyma cell. Banded filaments (arrows) appear in the fractured sieve pore. Some filaments appear on either side of the sieve plate (arrowheads) but because they tend to be obscured by ice crystals and frozen-out solutes (*Z*) it is not possible to say how uniformly they are distributed in the lumen. The distance between the apparent centres of filaments in the pores varies between about 100 Å and 500 Å. The diameter of filaments in pores on replicas appears to be between 100 Å and 250 Å; they cannot be distinguished from their shadows. But in sectioned and embedded material their diameter was measured more precisely as 163 Å (s.e.m. 3.2 Å, $n=79$) (Johnson[3]). Thus the space between the filaments in the pores is, at most, 500 Å. If this spacing is typical of translocating sieve pores then the pressure-flow hypothesis is inadequate[4,5]. So far I have seen twenty-nine pores in eleven sieve plates, and ten of these pores contained filaments spaced much as those in Fig. 1, eight pores contained some filaments whose spacing could not be determined, and eleven pores were not fractured or shadowed clearly enough inside to show whether they contained any filaments.

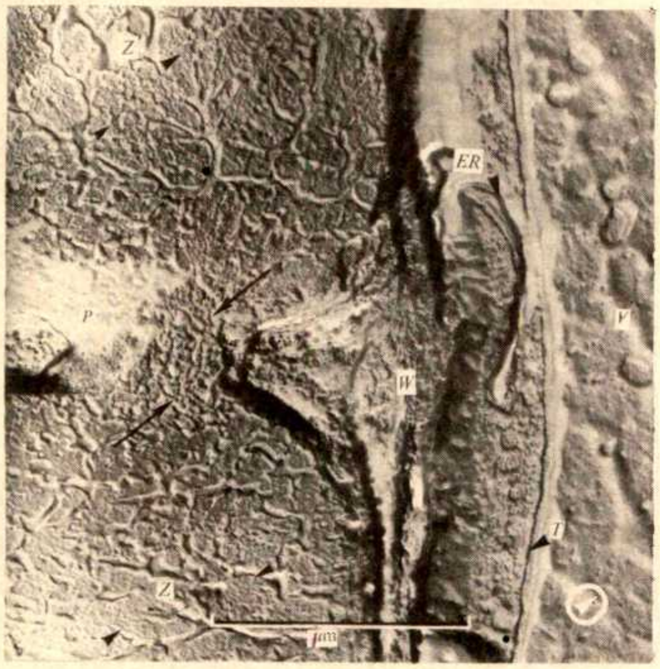

Fig. 1 Part of a sieve plate with a fractured sieve pore containing banded filaments (arrows), filaments nearby in lumen (arrowheads), plasmalemma (*P*), frozen-out solutes (*Z*), and part of an adjacent parenchyma cell with cell wall (*W*), vacuole (*V*), tonoplast (*T*), and endoplasmic reticulum (*ER*). The encircled arrow shows in which direction platinum carbon was applied.

There was no sign of any membranous transcellular strands as proposed by Thaine. Neither did any membranes which could be interpreted as boundaries or inner parts of such strands appear in the lumen of any sieve element. There was no sign of a tonoplast-like membrane in sieve elements[8,10,13] though tonoplast and endoplasmic reticulum appeared in nearby parenchyma cells (Fig. 1, *T* and *ER*). But fractured plasmalemma with particles did appear in surface view on sieve plates and lining sieve pores (Fig. 1, 2, *P*). Also, membranes of plastids appeared clearly in sieve elements (the plastids, not shown here, are about twice the diameter of the sieve pores and too large to pass through them). If there had been membranes in or around any transcellular strands lying through freeze-etched sieve pores in the study described here, they would have been obvious; transvacuolar membranes are obvious in freeze-etched phloem parenchyma cells even when the cytoplasm and vacuoles are distorted by large ice crystals (ref. 3, Fig. 15). Membranes in freeze-etched cells generally show up clearly whether fractured across or along their surfaces[14].

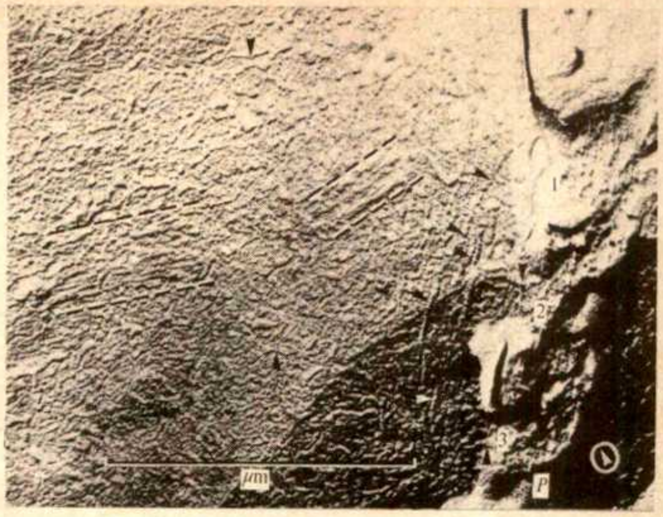

Fig. 2 Part of a sieve plate showing parts of three pores (1, 2, 3) with banded filaments near pores (for example, at arrowheads) and bundles or strands of filaments in the lumen (between broken lines). *P*, Plasmalemma.

Short bundles of filaments appeared near some sieve plates (Fig. 2, between broken lines), sometimes with separate filaments nearby (for example, at arrowheads). Such short pieces of bundle would appear if the long strands shown under the light microscope by Thaine and his co-workers[6,7] are, in fact, bundles of parallel filaments. In the electron microscope such bundles would only show their full length if they happened to run exactly along the plane of a fractured surface, or within the thickness of a thin section. The bundles seen (Fig. 2) had a boundary only in the sense that a hank of hair has a boundary. Their appearance does not support suggestions[4,8,9,15] that filaments in sieve elements might be organized to form semipermeable, or peristaltic, membrane-like tubes.

There now seems little doubt that fine bundles (strands or fibrils) of parallel filaments do occur in sieve elements[13,16–18] and that these are the transcellular strands seen under the light microscope. My study shows that they can occur in sieve elements that are undamaged by fixatives or release of turgor pressure. The function of these bundles remains obscure, though they have been likened[4,17–19] to fibrils thought to promote movement in other kinds of cells.

As membranous transcellular strands fail to appear in *N. peltata* in mature sieve elements in vascular bundles frozen rapidly while translocating, it seems unlikely that translocation generally depends on such structures. The notion that transcellular strands in sieve elements are bounded by membranes or contain elaborate systems of membranous tubules essential to translocation should be discarded. It has been premature to promulgate speculative mechanisms based on hypothetical membranous transcellular strands for which there is no evidence.

The close spacing of filaments in sieve pores shown here confirms the close spacing seen in carefully prepared sections[1,3,12]. It casts doubt on the adequacy of the Münch pressure-flow hypothesis and suggests that there must be pumps at places along sieve tubes.

I thank Mr D. A. John, Mr I. McRae, and Mr C. Verdan for technical assistance and Dr B. T. Watson for help with ^{14}C. This work was supported by a grant from the Science Research Council.

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Rapid Nitrosation of Phenols and its Implications for Health Hazards from Dietary Nitrites

THE use of sodium nitrite as a food preservative is under close scrutiny because its presence may result in the formation of secondary N-nitrosamines, which are powerful carcinogens in laboratory animals[1,2]. They may form either in the food itself during processing[3] or in the digestive tract from suitable amino compounds[4-6]. Only minute amounts of secondary N-nitrosamines, however, have been detected in preserved food so far[7].

But another reason for careful consideration of dietary nitrite levels arises from an interaction with phenolic compounds, again either in food processing or in the digestive tract. The carcinogenicity of aromatic nitroso compounds has not been widely examined, but *p*-nitrosophenol is listed by the Chester Beatty Research Institute as potentially dangerous[8] (possibly because of its metabolic reduction to an hydroxylamine), and preliminary evidence suggests that 1-hydroxy,2-nitrosonaphthalene causes hepatomas in rats[9]. Unfortunately, there is less information about the carcinogenicity of nitrosophenolic compounds than for nitrosamines, but there is clear-cut evidence that the nitrosation of phenolic compounds is much easier than that of most secondary amines. The latter are present in the digestive tract largely as their conjugate acid species ($R_2NH_2^+$) and are therefore unreactive, whereas phenol, for example, undergoes nitrosation readily by a *p*H-independent pathway from *p*H 1 to 5[10]. This difference is illustrated by comparable pseudo first-order rate coefficients (rate $=\bar{k}$ (substrate)) at *p*H = 1.5 and 25° C for the interaction of dimethylamine[11] (to form N-nitrosodimethylamine) and phenol (B. C. C. and R. J. Higgins, unpublished) (to form *p*-nitrosophenol) with 3×10^{-3} M sodium nitrite (Table 1). It is evident that phenol reacts about 10^4 times more rapidly than dimethylamine. This large difference should prevail for most alkylamines and be virtually independent of acidity up to *p*H = 5; it should be even greater for polyhydroxylated (for example catechol) and polycyclic (for example 2-naphthol) aromatic compounds, both of which are more reactive towards nitrous acid than phenol. Further, the dietary intake of phenolic compounds is probably much larger than secondary amines, because the former are common constituents of both plant (flavones, quinones and so on) and animal (adrenaline, tyrosine, tryptophan and so on) material. Of possibly greater significance is the estimated 42 mg–300 mg of phenolic material produced each day by the stomach via the gastric juice[12].

Table 1 Nitrosation Rates for Dimethylamine and Phenol at *p*H=1.5 and 25° C

Substrate	$10^2\times k$*	$10^4\times\bar{k}$† min^{-1}
Dimethylamine	1.88 $min^{-1}\ mol^{-2}\ l^2$	0.0019
Phenol	65.4 $min^{-1}\ mol^{-1}\ l$	20

* For dimethylamine, $v=k$ (total dimethylamine) $[HNO_2]^2$; for phenol $v=k$ (total phenol) $[HNO_2]$.

† From k assuming $[HNO_2]=3\times10^{-3}$ M, close to the expected concentration in the human stomach for foodstuffs containing the statutory US $NaNO_2$ limit of 200 p.p.m.

It is evident that the implications of using nitrite salts as a food preservative are wider than their relation to the formation of secondary N-nitrosamines. Conversely, if nitrosophenols prove to be harmless, then phenolic compounds present in both the diet and the gastric juice may effectively remove nitrite salts before they have a chance to interact with any secondary amines or other nitrogenous material from which N-nitrosamines may form.

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Reference Abbreviations

FROM September 1 it is *Nature's* intention that all abbreviations of references should conform to the style of the *World List of Scientific Periodicals*, fourth ed. (Butterworth, 1963–65). The changeover will be gradual and authors submitting manuscripts from now on are asked to ensure that the references are written appropriately.

BOOK REVIEWS

The Roots of Ethology

The Animal in its World: Explorations of an Ethologist, 1932–1972. By Niko Tinbergen. Volume I. *Field Studies.* Pp. 343. (George Allen and Unwin: London, February 1972.) £6.35.

THIS delightful book needs no praise, for it stands firmly upon its obvious merits and upon the reputation of its author. It consists of reprints, or translations, of ten of Niko Tinbergen's well known studies of animal behaviour in the field, spanning forty years of investigation (1932–72). Some of these papers are "classic" and will already be known to all well-read ethologists. But not all of them are now easy of access, and it will be a great convenience to many ethologists to have them readily available in this new format. There is another great advantage, however, in the production of this volume—this is that the papers are so readable and intriguing, in a way so delightfully simple and yet so profound and, above all, so redolent of the open air, that there are innumerable field naturalists and other non-specialists who will find them eye-opening as well as refreshing and stimulating to the mind.

The four earlier papers deal with the behaviour of two insects—the bee-hunting digger wasp (*Philanthus*) and the grayling butterfly (*Eumenis*). Three others are concerned with the black-headed gull, one with comparative studies of several species of gull and in addition there is a delightful study of food-hoarding by the fox. Finally there is a consideration of the advantages to small defenceless animals of living "scattered" rather than in crowded groups or colonies.

But in addition to all this the book is of interest to historians of biology in that it displays the research course followed by one of the pioneers of ethology. The dust cover links Niko Tinbergen and Konrad Lorenz as jointly the founders of "the young science of ethology". In a sense this is true in that both of them have been prime movers, in the period of forty years covered, in securing the establishment of ethology as a separate, respectable and inevitable branch of animal biology. It is also quite clear, from what both Tinbergen and Lorenz have from time to time said, and indeed from what the former says in this book, that though indeed originators they are also in large measure canalizers. Many of the essential concepts of modern ethology can be found long before these two came upon the scene in the writings of Jakob von Uexküll and Oscar Heinroth in Germany; of Lloyd Morgan and Julian Huxley in Great Britain; and still more remarkably of C. O. Whitman, Wallace Craig, William Morton Wheeler and Karl Lashley in the USA. Yet Konrad Lorenz is rightly regarded as the founder of "modern ethology" in that he alone succeeded in welding these concepts together to form an effective general theory of animal behaviour. And it was largely due to his doing this that ethology graduated from being a conglomeration of isolated, albeit fascinating, studies of the field biology of individual animals, to become a really comparative science. So it is interesting to see in this volume the change of emphasis that occurs in Niko Tinbergen's work after the critical year 1938, when he and Lorenz first worked together. That brief period of collaboration in Altenberg, Austria, was rudely shattered by the coming of the Second World War, which in due course sent Konrad to a prison camp in Russia and Niko to a German hostage camp in Holland. And it was ten years before they came together again on a moving occasion in Cambridge.

From then on much of Tinbergen's work consisted, in fact, of field and experimental demonstrations and investigations of many of the features in the Lorenzian system which were, in Konrad's case, based on immensely percipient observation of animals and his ability to "know" a great variety of species, rather than on experimental studies undertaken by himself.

The fascinating early studies of Tinbergen on insect behaviour stem more from that remarkable "Baltic Baron" Jakob von Uexküll, the title of whose great book, *Umwelt und Innenwelt der Tiere*, is, as near as makes no matter, the same as that of the book we are reviewing. Equally important as forerunners were Karl von Frisch in Austria and Mathilde Hertz in Germany and later England. It was these three, rather than Heinroth and Julian Huxley, who were the chief "mentors" of the young Tinbergen. But for the historian of science, the great puzzle is—why did American zoologists, having been shown the way so clearly by their own great pioneers, require a transfusion of blood from Europe before they could really get under way? For the USA could easily have been first in the field. Thus in 1898 Charles Otis Whitman[1,2] said "Instincts and organs are to be studied from the common viewpoint of phyletic descent." Not only did he say this, he also systematically studied and evaluated instincts as taxonomic characters. He did this notably with the doves (*Columbidae*) and also extensively with the leech, *Clepsine*, and the mud-puppy, *Necturus*. Then in the ten years from 1908 Wallace Craig produced seven or eight seminal papers. Yet when I was in Harvard in 1951–2, giving a course of lectures covering modern developments of animal behaviour studies, a much aged Wallace Craig was present. But as far as I could find out, only two people in a large audience knew who he was and what he had done; and only one of them knew that he had been living in Cambridge, Mass., for years! Again in 1902 that great entomologist William Morton Wheeler wrote[3] "The only term hitherto suggested which will adequately express the study of animals with a view to elucidating their true character as expressed in their physical and psychical behavior towards their living and inorganic environment, is ETHOLOGY". And fifteen years later he wrote a brilliant chapter on instincts[4]. (Not published until 1931.) Yet coming even from him, the greatest living authority on the instinctive behaviour of ants and other social insects, the seed fell on stony ground! Again J. B. Watson in 1908[5] produced a classic monograph on the behaviour of noddy and sooty terns; and later Watson and Karl S. Lashley[6] collaborated on the same subject. Then in 1938 Lashley[7] produced a famous paper which contained almost all the central ideas of the Lorenzian ethology, but piecemeal and not properly coordinated. The more we look into this the deeper the mystery seems to be. But I think one can suggest at least one clue, which perhaps gives us the answer. From 1898 to 1911 Thorndike, primarily a psychologist, produced and elaborated his study based upon observations of cats in "puzzle-boxes"[8], entitled "An experimental study of the associative processes in animals." This led to a theory of animal behaviour which was quickly taken up by J. B. Watson and became known as "behaviourism". This was fundamentally associationist or "mechanist" in outlook and prided itself upon being purely objective—with the implication perhaps that it was more nearly a physiological than a psychological system. (This claim to objectivity was also a characteristic of Tinbergen's writings on ethology after his first contact with Lorenz.) I think perhaps we should not have heard so much of Watson's behaviourism had it not been that, within a few years of its publication, the work of Pavlov and Bekhterev began to be known outside Russia. And so for the first time there seemed to be a physiological system that could be related in detail to the superficially physiological ideas behind behaviouristic psychology. Behaviourism was in some ways a laudable attempt to be objective and purge behavioural study of the uncritical anecdotal writing previously so much in evidence; but behaviourism as a general theory of animal behaviour was woefully inadequate—a fact of which anyone must be convinced who tries today to read Jacques Loeb on tropisms, taxes and the like. But I think the tremendous success and obviously immense importance of Pavlovian conditioning in the form in which it struck the United States through Watson, but from which his old colleague Lashley vigorously dissented, may well explain the prolonged period of hibernation of the indigenous American ethology.

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Survey of Syntheses

Theory and Experiment in Exobiology. Edited by Alan W. Schwartz. Volume 2. Pp. 146. (Wolters-Noordhoff: Groningen, The Netherlands, 1972.)

THE levels of argument and explanation in this serial publication suggest that its object is to inform experts about novel concepts and observations relevant to the history, nature and distribution of life. The editor might with advantage follow the example set by editors of other "Annual Reviews" and assume that readers are already familiar with background information. Textbooks and semi-popular articles could cater for the needs of those who are less well informed. If the editor feels that this serial must cater for the needs of all, a great deal of space would be saved if each issue contained a catalogue, or syllabus, of subjects about which knowledge is being assumed in the main body of the text: for example, that there are probably many planets like this one; that complex molecules such as amino acids and purines are formed by non-biological processes in reducing environments; that they will polymerize spontaneously; and that it is possible to imagine a form of "evolution" by selection among molecules during the probiotic phase of a planet's history. If something like that were done, material scattered here over about 50 pages could be compressed into two or three. Such a plan would not only save space, it would also encourage contributors to think more clearly about the novelty of what they were saying. General surveys and syntheses have their place—a new generation is always coming along that has to be told the old stories—but they are out of place in a regularly-appearing review journal. Possibly the editor has an inkling that all is not well. Hitherto, articles were solicited, now ". . . a cautious invitation (is extended) for contributed material from readers of this series. It is suggested that potential contributors outline their proposed article by means of a letter before undertaking it".

Three articles deal specifically with exobiology. Alexander complains that the possibility of back-contamination if samples are returned from a landing on Mars "has received essentially no consideration. . . ." It may be that the proposed quarantine routines are inadequate, and that a more extensive menagerie and garden should be used to test for dangerous organisms, but scientists and science fiction writers recognized the risk long ago. Mitz describes recent developments in automated life-detection systems to be used on Mars. These will probably be adequate provided any organisms there are so considerate as to use biochemical systems similar to our own. Steinman is a little more broadminded and, like Pflüger a century ago, directs attention to the cyanides.

The other three articles deal with the origins of life. Allen suggests that we now have a macromolecular obsession, and that life-like activities among substances with molecular weights around 500 (which he calls bions) should be considered. So far, his attempts to detect such activities have failed. Lacey and Fox argue that origins are to be sought among proteins or proteinoids, that RNA preceded DNA, and that the original "genetic code" made stereochemical sense but has become a "code" as a result of selection for precision. I liked their gnomic comment: "Concepts must, however, be logical, whereas new facts are not required to meet such a standard." Hall, Cammack and Rao think that the ferredoxins were important enzymes during the anaerobic phase of earthly life, and that evidence about the early course of evolution can be got by comparing their amino acid sequences. This concept leads them to a plausible system of phylogeny and gives some support to the idea that eukaryotes evolved by symbioses among prokaryotes.

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More Environment

The Science of the Total Environment. Edited by E. I. Hamilton. Volume 1. No. 1. Pp. 115. (Elsevier: Amsterdam, May 1972.) Dfl 91.00, $26.75 (published quarterly).

A NEW journal of the "environment" perhaps needs some justification in view of the quite prolific literature now existing on this nebulous but popular topic. It is a pity that *the science of the total environment* (the lower case presumably indicating the "key" in which contributions are intended to be written) does not have an introduction in the first issue expounding the intended principles and scope of the journal. As it stands, almost any article on the physical or life sciences could be accepted, yet many of the contributions indicate a considerable specialization within the topics discussed which seems at variance with this principle of generality. Nevertheless, the eminence of the editorial board means that papers of high quality are to be expected in this journal and the issues, so far, live up to this hope.

Several papers appear on trace element analyses, notably an extension of Samsahl's classical work on automatic chemical activation analysis and a valuable progress report by the editor on a detailed study of problems in trace element analysis. In a totally different area, a wide ranging review of potential chemical hazards from drugs, feed additives, pesticides and industrial agents is presented by Fishbein and Flann. Other articles range from measured biological effects of pesticides and similar substances to various chemical and physical aspects of air and water pollution.

Altogether the new journal seems a worthwhile venture provided it does not become submerged in a flood of similar publications. L. SALMON

Exhaustive Physics

Handbuch der Physik/Encyclopedia of Physics. Herausgeber S. Flugge. Gruppe 3: Mechanisches und Thermisches Verhalten der Materie. Band 6a, Teil 2: Festkopermechanik 2/Mechanics of Solids 2. Edited by C. Truesdell. Pp. x+745. (Springer: Berlin and New York, 1972.) 288 DM; $91.30.

THIS large volume contains six articles dealing with various aspects of the theory of elasticity and closely related topics. It is presumably intended to supplement Vol. 6 of the "Encyclopedia of Physics" entitled "Elasticity and Plasticity" which was published in 1958. In addition to an article by Sneddon and Berry on classical elasticity, that volume contains contributions on photoelasticity, inelastic continua, rheology, fracture and fatigue. The present volume, in contrast, is concerned exclusively with theoretical solid mechanics, and almost entirely with elastic solids.

All of the contributions are substantial, but two of them are major works dealing exhaustively with important branches of the subject, and amounting to considerable monographs in themselves. The first of these is by M. E. Gurtin and is entitled "The linear theory of elasticity". Professor Gurtin states his purpose as being to "give an exhaustive presentation of the linear theory of elasticity", and he proceeds to do exactly that. His words, however, are intended to be interpreted strictly literally; the treatise is concerned exclusively with the development of the theory and the statement and proof of theorems in it. Applications play no part whatsoever in the presentation. The main chapters of the article deal respectively with the formulation of the linear theory of elasticity, elastostatics, and elastodynamics. The treatment is certainly exhaustive; every theorem and result in linear elasticity of which I am aware is included, and very many more besides. Even more pleasing is the clarity of the presentation. Professor Gurtin has achieved the rare feat of being simultaneously rigorous and readable. This can only be described as a brilliant account of linear elasticity theory which will surely become the standard reference work in that subject for many years to come.

The other long article is by P. M. Naghdi on the theory of plates and shells. The first problem which confronts any writer on this subject is to decide whether to develop the theory by the direct approach, in which the shell is treated as a directed two-dimensional deformable surface, or by approximations from the equations for three-dimensional deformable bodies. Professor Naghdi resolves this dilemma by developing both formulations in parallel. This approach gives many insights into the theory, and invites interesting comparisons of these two ways of formulating it which the author does not neglect to discuss. Inevitably, this dual formulation adds considerably to the length of the article, so that at times the rate of progress seems a little slow. The main chapter headings are kinematics of shells and plates, basic principles for shells and plates, elastic shells, linear theory of elastic plates and shells. There is an appendix on the geometry of a surface and related results. The theory developed is a thermodynamical theory. A complete account is given of elastic plates and shells, but there is very little reference to inelastic materials. This article also is concerned exclusively with the development of theory, and includes no discussion of applications. It collects together much of the recent work on the subject, as well as some not previously published, and will be a valuable work of reference for all who are interested in the foundations of the theory of plates and shells.

Similar comments can be made about the shorter, but still substantial, article by S. S. Antman on the theory of rods. This also formulates the theory both by approximation of three-dimensional equations and as a director theory. Some problems for non-linear elastic rods, mostly of a rather general nature, are also discussed. The article by D. E. Carlson on linear thermoelasticity follows that by Gurtin both in the book and in spirit. Although likely to be overshadowed by its predecessor, it nevertheless gives a clear and rigorous account of its subject and is a welcome contribution to the volume. The remaining two articles (the shortest two in the book) are both by G. Fichera and deal with existence theorems in elasticity. They are very mathematical in character even by the standards of this volume. Although they are presented in the context of linear elasticity theory, they deal with much more general problems in the theory of partial differential equations, and require a good knowledge of functional analysis from the reader.

The book as a whole will no doubt become a valued reference work, as an encyclopaedia should. The individual articles are excellent in their various ways, but they do not together amount to anything approaching a comprehensive account of elasticity. The emphasis throughout is very strongly on formulation and general theory. Applications are hardly anywhere mentioned, and a newcomer to the subject looking through the volume would scarcely be likely to realize that elasticity is, for good reasons, of interest to engineers and applied physicists. He might even wonder why it forms part of an encyclopaedia of physics. However, this is not a book for beginners, and it must be presumed that potential readers will have sufficient background knowledge to be able to recognize that there are many other aspects to the subject of elasticity besides those presented here, and will place the individual articles of the volume within this wider context. Such readers will find it a most useful addition to the literature, although few of them are likely to be able to afford to purchase it for themselves.

A. J. M. SPENCER

Gunn Diodes

Transferred Electron Devices. By P. J. Bulman, G. S. Hobson and B. C. Taylor. Pp. x+402. (Academic: London and New York, November 1972.) $26.50.

THIS book covers a substantial amount of background information on the microwave semiconductor devices commonly known as Gunn diodes. These devices depend on the transfer of electrons from a low mass, high mobility condition to a high mass, low mobility condition, when elevated electric fields are applied to n-type gallium arsenide, to generate or amplify microwaves.

The devices are already being widely used in broadly swept microwave oscillators, as low noise local oscillators, as power sources for intrusion alarms; and pulsed versions have been developed for limited range radars. The increase in the use of these devices from year to year shows that extremely high production volume of them will eventually exist.

The information presented in the book covers the physical fundamentals, the crystal growth and processing technology, the device-circuit interaction, and general and special applications of the devices. The level of the presentation is such that upper university level students and working professionals can easily learn the subject for the first time. It is also interesting reading and a valuable reference for anyone who is an expert in some aspect of the field. Such an expert will notice that recent results could not be included because of the usual publication delays. This is an inevitable problem in a fast moving field. It is now ten years since the first experimental results were obtained on these devices and thus it is necessary to document the ideas and the progress to help the many people now involved in the field.

The authors are to be especially praised on two aspects of the book. One aspect is the inclusion of numerous references, with an author index that includes nearly 300 names. The continuing development of this field will be carried out by many of the authors listed, so that a newcomer to the field will know who to contact for new information. The other aspect is that the authors made a strong, extra effort to become knowledgeable about those specialties of the field in which they had little experience. As a result, the total presentation is uniform and solid in all areas.

I highly recommend the book, especially to all those people new to the field, and would suggest that it be used in advanced courses on the subject.

L. F. Eastman

Ring Systems

Inorganic Rings and Cages. By D. A. Armitage. Pp. 387. (Edward Arnold: London, December 1972.) £12.50.

This book will inevitably invite comparison with Allcock's *Heteroatom Ring Systems and Polymers* (Academic Press, New York and London, 1967), and the exhaustive two-volume treatise by Haiduc, *The Chemistry of Inorganic Ring Systems* (Wiley, New York and London, 1970). Dr Armitage has confined himself to systems, rings or cages, which do not contain carbon, in contrast with the book by Allcock which, on the other hand, excludes homoatomic systems. The volume under review is more selective but less comprehensive than the one by Haiduc. It will therefore be up to the individual reader to decide which of these three volumes he prefers, as undoubtedly economic necessity will dictate some selectivity. This volume is of course the most up to date of the three and goes systematically right through the main group elements. I found the book most interesting and well worth reading. The literature is covered up to 1970 and each chapter contains an appendix including references from the 1971 literature. Obviously in a book of this size, there must be omissions and I noticed some, particularly in the fields with which I am most familiar. The volume is not always fully referenced and some of the references are placed in such a manner as to be misleading. Quite a number of the names in the reference lists have been misspelt. The book contains a formula index, a specific index of compounds, as well as a general index, but no author index. It is a stimulating, worthwhile book in a field which seems to have begun again to attract the amount of attention it really deserves. This and the other two comparable books all have their merits and are worth buying. Individual research workers and teachers will have to decide for themselves which of these most meets their specific needs.

R. A. Shaw

Crystal Defects

Defects in Crystalline Solids. By B. Henderson. Pp. xi+203. (Edward Arnold: London, December 1972.) £6 cloth ; £3 paper.

This is the first book to appear in a series entitled *The Structures and Properties of Solids,* edited by Professor B. R. Coles. The general level is appropriate for mature undergraduates and junior postgraduates in physics, chemistry, metallurgy and materials science. Dr Henderson's text is based on lectures delivered at the University of Keele, and is based towards point defects and small clusters rather than, as tends to be more common in books on defects in solids, towards dislocations and mechanical properties. Following the first chapter, which gives a general introduction to defects, five of the remaining seven chapters discuss point defects in ionic solids, semiconductors and metals. The final chapter describes the interaction of dislocations with other defects, and covers some aspects of slip and hardening. Defects induced both thermally and by radiation are discussed, although there is very little on radiation damage mechanisms as such.

The general layout of the book is good and the material chosen covers a wide range of defect properties. The principal criticism is that there is a large number of misprints and mistakes in the text and equations, which detracts from the usefulness of the book to a beginner in the subject. The experienced reader will easily notice the occasional error, but someone less familiar with the subject could have a frustrating time in places trying to sort his way through mixed notations and inconsistent equations. In one or two places the text is also a bit misleading. For example, the description of the formation of F_A centres in alkali halides is at variance with the presently accepted mechanism. How many of these shortcomings are due to the author and how many to the publisher is hard to decide, but in any event it is a great pity that an otherwise excellent book should suffer in this way.

The book should prove attractive to readers interested in receiving an introduction to the science of defects in solids, and it is to be hoped that a second edition will be produced with the errors corrected. A. E. Hughes

Sulphydryl Biochemistry

Biochemistry of the SH Group: The Occurrence, Chemical Properties, Metabolism and Biological Function of Thiols and Disulphides. By P. C. Jocelyn. Pp. xx+404. (Academic: New York and London, November 1972.) £6.50; $20.

This small book sets out to cover a very large field indeed. It deals with the properties and functions of low molecular weight thiols and disulphides; with SH and SS groups in proteins; with the occurrence and functions of these groups in various mammalian tissues, in microorganisms and in plants; and concludes with chapters on radioprotection and pharmacology. The author states that the book is intended primarily for first year university students. However, it is difficult to see how he could get so much information into one small volume in a form which is intelligible to students.

The first 100 pages cover the chemical aspects of the subject. After describing a wide range of naturally occurring thiols and disulphides (including proteins) the author goes on to deal with their physical properties, chemical reactions and methods of estimation. These chapters are good in parts but unfortunately one has to know the subject to know which parts are good. Thus Hopkin's early work on glutathione is given in some detail but the section on analytical methods is unbalanced and fails to give the reader a proper understanding of the principles on which the different methods are based. Equally, hydrogen bonding of sulphur and thiazoline ring formation, which cannot explain the phenomenon of the unreactive SH group, are given the same weight as hydrophobic bonding, which can.

The latter half of the book, which covers the biological aspects of the subject, suffers from the same deficiencies. Thus the chapter on thiols and disulphides in blood is adequate but the following chapters on their occurrence in animal and plant tissues are little more than lists of headings. The last two chapters on radioprotection and pharmacology could well have been omitted from a book of this level.

The bibliography, containing some 2,000 references, is large for a book of this size but inadequate for the field that is being covered. A sample check showed that one in five of the references contains errors (I am given two sets of initials).

This book could have been very valuable for students if it had covered a more limited field in greater detail and, above all, more critically. In its present form it is misleading for students and inadequate as a source of reference for research workers. R. Cecil

CORRESPONDENCE

Nerve Growth Factor

SIR,—Drs Hendry and Iverson (*Nature*, **243**, 500; 1973) report that surgical excision of submaxillary salivary glands in adult mice causes a profound temporary drop in the plasma and tissue concentration of nerve growth factor, which was followed by a fairly rapid recovery to approximately normal plasma concentration. They postulated that an unidentified source of NGF must have been available which was capable of maintaining normal plasma concentrations. Furthermore, it is known that NGF is absent from the mouse submaxillary glands during foetal and pre-adolescent life and attempts to isolate it from the glands of animals other than the mouse have been unsuccessful, and yet it is essential for the growth in culture of both sympathetic and sensory ganglia of many species. It would, therefore, be expected that another source of NGF should be available to foetal and pre-adolescent mice and other species of animal. Last year (*Exp. Cell Res.*, **74**, 170; 1972) we reported that fluorescent labelled anti-NGF stained intestinal mucosae of all the foetal and adult animals belonging to many species, including mice. In gel-diffusion the crude mouse intestinal homogenate produced two lines of precipitation against anti-NGF, one of which showed a reaction of identity with NGF. Although all our attempts to demonstrate nerve growth promoting activity in the crude homogenates were unsuccessful, it is possible that a sensitive assay technique like radioimmunoassay may be able to detect its presence in the intestine.

Yours faithfully,
S. KUMAR

Clinical Research Laboratories,
Christie Hospital,
Manchester

Obituary

Mikhail Dmitrievich Millionshchikov

ACADEMICIAN MIKHAIL DMITRIEVICH MILLIONSHCHIKOV, vice-president of the Soviet Academy of Sciences, deputy director of the Kurchatov Institute of Atomic Energy, and a leading spokesman for the Soviet Union regarding scientific contacts with the West, died on May 27, 1973.

Millionshchikov was born on January 15, 1913, in Groznyi in the Caucasus. He was educated at the Groznyi Petroleum Institute, where he graduated in 1932. By the time he was twenty, he had already attracted considerable notice with his research on problems of the filtration of oil and gas through rocks. In 1934, he became an instructor at the Moscow Aviation Institute, where he remained until 1943. Here he carried out research into the theory of turbulence, working initially under the supervision of the mathematician Andrei N. Kolmogorov, and obtaining some now classic results.

In 1943 he became an instructor at the Moscow Institute of Engineering and Physics and worked simultaneously at the Institute of Mechanics of the Soviet Academy of Sciences. He joined the Soviet atomic energy programme in 1949, working at the Kurchatov Atomic Energy Institute on various aspects of nuclear engineering, notably the direct conversion of nuclear energy into electrical energy. In 1960, on Kurchatov's death, he became deputy director of the Institute, continuing his research on nuclear reactors, direct conversion technology and low temperature plasmas.

He was elected a full member of the Academy of Sciences in 1962, becoming a vice-president of the academy in the same year. From that time onwards, he was greatly involved with organizational and training problems, and was especially concerned with the training of young scientists, the establishment of new science centres of the academy and the decentralization of research throughout the Soviet Union. In 1966, he became editor of the *Vestnik* of the academy.

Millionshchikov was a keen supporter and participant in the Pugwash movement, attending the first meeting in 1957 and becoming Chairman of the Soviet Pugwash Committee in 1964. In 1967 he became chairman of the Supreme Soviet of the Russian Federated Republic, and in both capacities was in an unusually privileged position for maintaining and strengthening scientific contacts with other countries. As early as 1970, he spoke publicly in favour of Soviet–American cooperation in space.

Millionshchikov's published works are relatively few, but his contribution to research in recent years, although classified, won him Lenin and State Prizes, and many Soviet honours and awards, including the Order of Lenin (four times) and the title of Hero of Socialist Labour (the highest Soviet civil award) in 1967. He also won several awards from other countries and was an honorary member of the Academy of Sciences of the German Democratic Republic and of the American Academy of Arts and Sciences.

Announcements

International Meetings

September 10–12, **First European Fluid Power Conference.** (The Secretary, First European Fluid Conference, National Engineering Lab., East Kilbride, Glasgow G75 0QU, Scotland.)

September 10–12, **Third Biennial Symposium on Turbulence in Liquids.** (Walter Ries, Continuing Education, University of Missouri-Rolla, Rolla, Missouri 65401, USA.)

September 10–12, **Conference on Differential Geochemistry and Its Applications in Engineering.** (The Secretary and Registrar, Institute of Mathematics and Its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY.)

September 10–13, **First National Quantum Electronics Conference.** (Dr R. C. Smith, Honorary Secretary, IOP Quantum Electronics Group, Electronics Department, The University, Southampton SO9 5NH.)

September 10–14, **Sixth International Mass Spectrometry Conference.** (C. H. Maynard, Administrative Secretary, Institute of Petroleum, 61 New Cavendish Street, London W1M 8AR.)

September 10–14, **Radioimmunoassay and Related Procedures in Clinical Medicine and Research.** (International Atomic Energy Agency, Karntner Ring 11–13, A-1011 Vienna, Austria.)

September 10–14, **IUPAC International Symposium on Macromolecules.** (Dr John F. Gibson, The Chemical Society, Burlington House, London W1V 0BN.)

September 10–16, **Seventh Congress of the International Union for Study of Social Insects.** (Dr P. E. Howse, Department of Zoology, The University, Southampton SO9 5NH.)

September 10–20, **Third International Congress for Virology.** (Professor P. Wildy, Department of Virology, Medical School, University of Birmingham, Birmingham.)

September 10–21, **Ambident Reactivity of Conjugated Systems.** (Dr P. W. Hickmott, Department of Chemistry, University of Salford, Salford M5 4WT.)

September 11–14, **Non-Silver Photographic Progress.** (Mr C. J. V. Roberts, Research Labs., Kodak Ltd, Wealdstone, Harrow, Middlesex.)

September 11–14, **British and German Pharmacological Societies Joint Meeting.** (Professor Dr Hans Herken, Pharmakologisches Institut der Freien Universität Berlin, 1 Berlin 33, Thielallee 69/73, Germany.)

September 12–15, **Sixth Congress of the Organ Transplantation Society.** (Organizing Secretariat, Studio MGR, Via Lanzine 40, I-202123, Milan, Italy.)

September 13–15, **International Orthopaedic Congress in Rotterdam.** (The Secretariat, c/o Holland Organizing Centre, 16 Lange Voorhout, The Hague, The Netherlands.)

September 13–15, **International Congress on the Knee Joint.** (Secretariat, c/o Knee Joint Congress, Medical Faculty of the Erasmus University, 50 Dr Molenwaterplein, Rotterdam, The Netherlands.)

September 16–20, **International Conference on Silicon Carbide.** (Professor J. W. Faust, Jr, College of Engineering, University of South Carolina, South Carolina 29208, USA.)

September 16–21, **Fifth International Fundamental Research Symposium.** (The British Paper and Board Makers' Association, Technical Section, Plough Place, Fetter Lane, London EC4.)

September 16–21, **Sixth Harden Conference.** (The Executive Secretary, The Biochemical Society, 7 Warwick Court, London WC1R 5DP.)

September 17–19, **BAGG Annual Conference.** (Dr J. C. Brice, Mullard Research Labs., Redhill, Surrey, England.)

September 17–20, **UK Automation Council, 5th Control Convention.** (The Conference Secretary, The Institute of Measurements and Control, 20 Peel Street, London W8.)

September 17–21, **International Chemical Conference.** (Dr E. R. Braithwaite, Climax Molybdenum Co. Ltd, Villiers House, 41–47 Strand, London WC2N 5JS.)

September 17–21, **Combustion Institute European Symposium.** (Dr A. R. Jones, Department of Chemical Engineering and Chemical Technology, Imperial College, London SW7.)

September 17–21, **Instrumentation, Control and Automation of Wastewater Treatment Systems.** (Mr A. Chandler, Secretary, UK Organizing Committee, Automation Workshop, c/o Greater London Council, Department of Public Health Engineering, 10 Great George Street, London SW1P 3AB.)

September 17–22, **International Biological Programme.** (Dr A. J. Holding, Department of Microbiology, School of Agriculture, University of Edinburgh, West Mains Road, Edinburgh EH9 3JG.)

September 18, **Autumn Conference and Annual General Meeting.** (The Association for High Speed Photography and the British National Committee for High Speed Photography, c/o Central Unit for Scientific Photography, Royal Aircraft Establishment, Farnborough, Hants.)

September 18–20, **Intermediates in Electrochemical Reactions.** (The Assistant Secretary, The Faraday Division, The Chemical Society, Burlington House, London W1V 0BN.)

September 18–20, **Electrofocusing Symposium.** (Dr J. P. Arbuthnott, Dept. of Microbiology, The University, Alexander Stone Building, Garscube Estate, Bearden, Glasgow.)

September 18–20, **Conference on Mathematics in Clinical Medicine.** (Secretary and Registrar, The Institute of Mathematics and Its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY.)

September 18–21, **Sixth International Meeting on Organic Geochemistry.** (Keith A. Kvenvolden, Chief, Chemical Evolution Branch, National Aeronautics and Space Administration, Ames Research Center, Moffett Field, California 94035, USA.)

September 18–21, **Conference on High Voltage Direct Current Transmission.** (The Institution of Electrical Engineers, Savoy Place, London WC2R 0BL.)

September 18–21, **Pore Structure and Properties of Materials.** (Technical University of Prague, Building Research Institute, Symposium RILEM/IUPAC Office, Solinova 7, 16000 Prague 6, Deivice, Czechoslovakia.)

September 19–20, **Conference on Environmental Engineering Problems in Industrialized and Developing Countries.** (Mrs Ann Cook, Conference Manager, Savoy Place, London WC2R 0BL.)

September 19–21, **Polymer Physics Group Biennial Meeting.** (Dr B. Jennings, Dept. of Physics, Brunel University, Uxbridge, Middlesex.)

September 19–21, **Colloid and Surface Chemical Aspects of Lubrication and Lubricants.** (Professor R. H. Ottewill, School of Chemistry, University of Bristol, Bristol BS8 1TS.)

September 19–21, **Biennial Polymer Physics Conference.** (Polymer Physics Group of the Institute of Physics, 47 Belgrave Square, London SW1X 8QX.)

September 19–23, **Oak Symposium.** (Mrs Mary Briggs, M.P.S., White Cottage, Slinford, Horsham, Sussex RH13 7RG.)

September 20, **Communities through Time.** (Dr J. E. Pollard, Geology Department, The University, Manchester M13 9PL.)

September 20–21, **Organization and Function of Microtubules and Microfilaments.** (Secretary of the Second International Congress on Cytopharmacology, Department of Pharmacology, University of Milan, Via Vanvitelli 32, 20129 Milan, Italy.)

September 20–21, **Symposium on Insect Flight.** (The Society's Registrar, 41 Queen's Gate, London SW7 5HU.)

September 20–21, **Properties of Building Materials.** (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX.)

September 20–21, **British Society for Cell Biology.** (Dr B. M. Richards, Searle Research Labs., Lane End Road, High Wycombe, Bucks. HP12 4HL.)

September 20–23, **Joint Geological Societies Meeting.** (Secretary of the Department of Geology, University of Manchester, Oxford Road, Manchester M13 9PL.)

September 20–28, **Fourth Symposium on Microdosimetry.** (Secretariat of the Fourth Symposium on Microdosimetry, Commission of the European Communities, DG XII—Biology Division, Dr H. G. Ebert, 200 Rue de la Loi, B-1040 Brussels, Belgium.)

September 21, **Meeting of the Chemical Society.** (Carbohydrate Group, Dr N. R. Williams, Chemistry Department, Birkbeck College, Malet Street, London WC1E 7HX.)

September 21–23, **Annual Conference of the British Society for the Philosophy of Science.** (Mr Larry Briskman, Department of Philosophy, David Hume Tower, George Square, Edinburgh EH8 9JX.)

September 22–27, **Fourth International Congress of Fodd Science and Technology.** (The Secretariat, IV Congress, Jaime Roig 11, Valencia 10, Spain.)

September 23–26, **Optical Properties of Thin Films.** (Dr H. G. Jerrard, Department of Physics, University of Southampton SO9 5NH, or Dr P. H. Lissberger, Department of Pure and Applied Physics, University of Salford M5 4WT.)

September 23–26, **ASLIB 47th Annual Conference.** (The Conference Organizer, ASLIB, 3 Belgrave Square, London SW1X 8PL.)

September 23–27, **Eighth International Conference on the Properties of Steam.** (The Secretary, UK National Committee on the Properties of Steam, 1 Birdcage Walk, London SW1H 9JJ.)

September 23–29, **International Conference on Kimberlites.** (Dr J. J. Gurney, Department of Geochemistry, University of Cape Town, Rondebosch, C.P., S. Africa.)

September 24–25, **Environmental Health Engineering in Hot Climates and Developing Countries.** (John Pickford, Department of Civil Engineering, University of Technology, Loughborough, Leics. LE11 3TU.)

September 24–27, **The Chemical Society Autumn Meeting.** (Dr John Gibson, The Chemical Society, Burlington House, London W1V 0BN.)

September 24–28, **Transduction Mechanisms in Chemoreception.** (T. M. Poynder, Secretary, Department of Physiology, University College, London).

September 24–28, **Noble Gases Symposium** (Dr A. Alan Moghissi, Chairman of the Program Committee, Noble Gases Symposium, US Environmental Protection Agency, P.O Box 15027, Las Vegas, NY 8114, USA.)

September 25–27, **First European Tribology Congress** (Eurotrip 73, Groups Department, The Institution of Mechanical Engineers, 1 Birdcage Walk, London SW1H 9JJ.)

September 25–27, **Computer Uses in Water Systems.** (The Water Research Association, Medmenham, Marlow, Buckinghamshire SL7 2HD.)

September 26–28, **Conference on Water Pollution Control Technology in Low Density Areas.** (Dr William J. Jewell, Department of Civil Engineering, University of Vermont, Burlington, Vermont 05401, USA.)

September 27, **Colloquium on Ion Exchange Chromatography on Amino Acids and Sugars.** (The Secretary of the Group, Dr E. Reid, Wolfson Bioanalytical Centre, Leapale Lane, Guildford, Surrey.)

Errata

In the article "Outbreeding and Inbreeding in a Zinc-Lead Mine Population of *Armeria maritima*" by C. Lefèbvre (*Nature*, **243**, 96; 1973), paragraph 8, line 3 and following, should read "If total inbreeding occurs the frequency of AA in the A-type progeny will be 0.25 (*not* 0.50). The potential amount of inbreeding in the population (7%) leads to the estimate that approximately 2% (*not* 4%) of AA plants must arise in the population."

In the article "Role of Erythrogenin from Liver and Spleen in Erythropoietin Production in the Anephric Rat" by C. Peschle, A. D'Avanzo, I. A. Rappaport, S. Russolillo, G. Marone and M. Condorelli (*Nature*, **243**, 539; 1973), Group 6 in Table 1 should read "Sham operation + nephrectomy + room pressure" instead of ". . . + hypoxia".

In the article "Apollo 17 'Orange Soil' and Meteorite Impact on Liquid Lava", by E. Roedder and P. W. Weiblen (*Nature*, **244**, 210; 1973), editorial change of the title and deletion of the opening paragraph have resulted in some confusion as to what the theory involves. The suggested mode of origin for this unusual soil, which differed from those suggested by the other groups working on it, is by meteorite impact on liquid lava containing olivine phenocrysts. Also, section (2) should read, "The olivine phenocrysts. These effectively preclude the first and the third of the three mechanisms of origin suggested above."

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Aspects of the Crusades: a Phased Historical Case Study in Problem Solving and Decision Making. By Michael Hamilton. (The Decisions of History.) Pp. 42. (London: Academic and Business Monographs, Ltd., 6 Brodrick Road, SW17, 1973.) [93

Rheumatism and Arthritis in Britain. Pp. 44. (London: Office of Health Economics, 1973.) 25p. [93

Bulletin of the British Museum (Natural History). Geology. Vol. 21, No. 2: Postcanine Occlusion in Cynodonts and Tritylodontide. By A. W. Crompton. Pp. 27–71 + 7 plates. £3.40. Vol. 22, No. 1: The Classification and Natural History of *Theropithecus* (*Simopithecus*) (Andrews, 1916), Baboons of the African Plio-Pleistocene. By Clifford J. Jolly. Pp. 1–123 + 20 plates. £6.65. Vol. 22, No. 2: Llandovery Conodonts from the Welsh Borderland. By R. J. Aldridge. Pp. 125–231 + 9 plates. £4.45. Vol. 22, No. 3: A Revision of the Redfieldiform and Perleidiform Fishes from the Triassic of Bekker's Kraal (South Africa) and Brookvale (New South Wales). By P. Hutchinson. Pp. 233–354. £4.30. Vol. 22, No. 4: Lower Palaeozoic Green Algae from Southern Scotland, and their Evolutionary Significance. By Graham Francis Elliott. Pp. 355–376 + 10 plates. £1.85. Vol. 22, No. 5: The Buchanosteid Arthrodires of Australia. By Errol I. White and Harry A. Toombs. Pp. 377–419 + 9 plates. £2.65. Vol. 22, No. 6: Planktonic Foraminifera from the Palaeocene-Eocene Succession in the Rakhi Nala, Sulaiman Range, Pakistan. By B. K. Samanta. Pp. 421–482 + 15 plates. £3.55. Vol. 22, No. 7: *Megistotherium*, Gigantic Hyaenodont from Miocene of Gebel Zelten, Libya. By R. J. G. Savage. Pp. 483–511 + 4 plates. £1.70. Vol. 22, No. 8: Introduction to the Miocene Mammal Faunas of Gebel Zelten, Libya. By R. J. G. Savage and W. R. Hamilton. Pp. 513–527. 60p. Vol. 23, No. 1: Marsupialia, Inscotivora, Primates, Creodonta and Carnivora from the Headon Beds (Upper Eocene) of Southern England. By P. E. Cray. Pp. 1–102 + 6 plates. £4.45. Vol. 23, No. 2: Some British Cretaceous Hastropods Belonging to the Families Procerithiidae, Cerithiidae and Cerithiopsidae (Cerithiacea). By H. L. Abbass. Pp. 103–175 + 8 plates. £3.45. (London: British Museum (Natural History), 1972 and 1973.) [24

Department of the Environment and the Welsh Office. Structure Plans: The Examination in Public. Pp. 12. (London: Department of the Environment and the Welsh Office, 1973.) *Gratis*. [24

Rutherford: The Father of Nuclear Energy. By Professor T. E. Allibone, CBE, FRS. (The Rutherford Lecture delivered on 3 November 1972 at the Polytechnic of Central London.) Pp. 24. (Manchester: Manchester University Press, 1973.) 48p net. [24

Queen Mary College (University of London). Annual Report, Session 1971–72. Pp. 168. (London: Queen Mary College, 1973.) [24

European Invertebrate Survey. Provisional Atlas of the Insects of the British Isles. General Editor: John Heath. Part 2: Lepidoptera (Moths—Part One). Edited by John Heath and Michael J. Skelton. Pp. 3 + 102. (Abbots Ripton, Huntingdon: Biological Records Centre, Monks Wood Experimental Station, 1973. Sole Agents: E. W. Classey, Ltd., 353 Hanworth Road, Hampton, Middx.) £1. [24

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(c) have already had substantial experience in cancer research or have demonstrated their potential to direct and conduct such research;
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(e) wish to teach medical and science graduates and undergraduates and to supervise postgraduates.

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for the *Zoological Record*, a bibliography of the world's zoological literature. Duties include scanning literature and indexing of relevant material.

Applicants should possess a degree in Zoological, Linguistic ability and previous experience in information work would be helpful but not essential. Posts based at the units at the National Lending Library, Boston Spa, and the British Museum (Natural History).

Salary £1,298 on scale to £1,832.

Applications in writing to:

Establishment Officer,
Zoological Society of London,
Regent's Park,
London NW1 4RY,

by August 25, 1973. (307)

UNIVERSITY OF DUNDEE

Applications are invited from Biochemists holding an honours degree or its equivalent (e.g., B.Med.Sci. in Biochemistry) for a post of

RESEARCH ASSISTANT

in the Departments of

PSYCHIATRY and BIOCHEMISTRY

The successful candidate will be involved in investigations of biochemical factors in depressive illness in association with Dr G. J. Naylor and Dr D. A. Stansfield. The post is available for three years from October 1, 1973. Salary £1,419 to £1,560 to £1,704 per annum.

Applications containing the names and addresses of three referees, and quoting Ref. EST/60/73J, should be sent to the Secretary, University, Dundee DD1 4HN, not later than August 31. (254)

UNIVERSITY OF NAIROBI

KENYA

Applications are invited for following posts in DEPARTMENT OF BIOCHEMISTRY:

ASSOCIATE PROFESSOR. Applicants should have a Ph.D. and extensive experience in teaching and research. Appointee will be required to teach courses to students of Medicine and Science. Preference will be given to Biochemists who have specialised in fields such as endocrinology, molecular biology or enzymology.

2 SENIOR LECTURERS. Applicants should have a Ph.D. in Biochemistry. Appointees will be required to teach students of Science and Medicine, direct student research projects and assist graduate students in preparation for M.Sc. and Ph.D. degrees. Preference will be given to candidates with research experience in microbiological chemistry, enzymology and neurochemistry. Administrative experience will be an added advantage.

2 LECTURERS. Candidates should have a Ph.D. and will be required to teach students of Medicine, Science, Veterinary Medicine and Agriculture. Research experience in enzymology, immunology and mitochondrial function will be an added advantage.

The Department has modern equipment for enzyme and radio-isotope work, gas liquid chromatographs, high speed centrifuges, recording spectro-photometers and spectro-photofluorimeter, permitting joint projects with clinical and other pre-clinical departments.

Salary scales: Associate Professor K£3,036-K£3,564 p.a. Senior Lecturer K£2,256-K£3,036 p.a. Lecturer K£1,500-K£2,580 p.a. (K£1=£1.14 sterling). The British Government may supplement salaries in range £450-£1,050 p.a. (sterling) for married appointees or £150-£750 p.a. (sterling) for single appointees and provide children's education allowances and holiday visit passages. F.S.S.U. Family passages; various allowances.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail, not later than September 13, 1973, to the Registrar, University of Nairobi, P.O. Box 30197, Nairobi, Kenya. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of the appointment may be obtained from either address. (322)

UNIVERSITY OF IBADAN

NIGERIA

Applications are invited for the following posts in DEPARTMENT OF AGRONOMY:

LECTURER IN SOIL SURVEY AND CLASSIFICATION. Candidates must have a Ph.D. in Soil Science, particularly a major in Soil Survey with a minor in Soil Classification. They must have working knowledge of field work and must be conversant with tropical soils. Appointee will be required to supervise postgraduate students in his field and will be expected to teach undergraduate and postgraduate courses.

LECTURER IN CROP PRODUCTION. Candidates must possess a doctorate in Agriculture in the field of Crop Production. They must possess a working knowledge of production practices of field crops such as cereals, fibre crops and tubers. They should be conversant with tropical crops. Appointee will be required to supervise postgraduate students in his field and will be expected to teach undergraduate and postgraduate courses. He should have sufficient field experience with a sound knowledge of agricultural statistics.

TECHNICIAN. Candidates must possess HNC in Chemistry, a Certificate of the Royal Institute of Chemistry, in advanced and Analytical Chemistry and should have wide experience in running laboratories for routine analyses of plant materials and must be able to maintain and handle sophisticated equipment. They must have enough experience in working and organising a laboratory and be able to control a sizeable laboratory staff.

Salary scales: Lecturer N2,760-N4,830 p.a. Technician N2,140-N3,060 p.a. (£1 sterling=N1.62). The British Expatriates Supplementation Scheme is unlikely to be applied to this appointment. Family passages; various allowances; superannuation scheme; biennial overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than September 17, 1973, to the Registrar, University of Ibadan, Ibadan, Nigeria. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address.

(323)

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF CIVIL ENGINEERING

Applications are invited for the post of RESEARCH ASSISTANT to carry out investigations relating to the mathematical modelling of the Solent and its applications, working under Dr C. A. Brebbia.

Starting salary will be up to £2,079 per annum. Candidates with a good honours degree and some relevant experience will be preferred.

Applications, together with a brief curriculum vitae and naming two referees, should be sent to the Deputy Secretary's Section (ext. 2400), the University, Southampton SO9 5NH as soon as possible. Please quote reference No Na 107/R. (259)

Department of Health and Social Security British Pharmacopoeia Commission, London W1

Chemists/ Pharmacists

■ Investigate proposed specifications for establishing identity, purity and potency of medicinal chemicals ■ Devise methods of analysis ■ Report to technical committees ■ Laboratory will be moving to Canons Park, Edgware.

□ Degree, HNC or equivalent in Chemistry or Pharmacy □ Practical experience in quality control an advantage □ Age under 30 □ Appointment as Higher Scientific Officer (£2251-£2842) or Scientific Officer (£1493-£2352) □ Ref: SB/1/KD □ Closing date 7 September 1973.

□ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Ministry of Agriculture, Fisheries and Food London Pests Unit, Aldgate, E1.

Biologists

■ 3 posts on team which advises on infestation control in London area ■ Inspect food and other stored products, particularly imports, for insect infestation ■ Advise food and farming industries ■ Advise bodies concerned with public health and train staff ■ Control insects and rodents in Crown properties ■ Liaison with Pest Infestation Control Laboratory ■ Some lecturing involved.

□ Degree, HNC or equivalent in biological subject □ Driving ability desirable □ Age under 27 □ Appointment as Scientific Officer (£1,493-£2,352) □ Ref: SB/3/AF □ Closing date 7 September 1973.

□ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Ministry of Agriculture, Fisheries and Food Pest Infestation Control Laboratory, Tolworth, Surrey.

Chemist/ Physicist

■ Join small team within Bio-Chemistry Section providing Mass Spectrometric service to this and other Ministry laboratories ■ Identify pesticide residues in tissues of wildlife casualties caused by agricultural chemicals ■ Take charge of day to day running of AEI MS.30 Double Beam Instrument ■ Scope for development work and original investigations.

□ Degree, HNC or equivalent in Chemistry or Physics □ Experience of spectroscopic techniques advantageous – particularly practical application of mass spectrometry □ Age under 27 □ Appointment as Scientific Officer (£1,408-£2,267) □ Ref: SB/2/AF □ Closing date 7 September 1973.

□ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Department of Trade and Industry Warren Spring Laboratory, Stevenage, Herts.

Analytical Chemist

■ Instrumental and classical analysis in support of research into mineral processing, metals extraction and environmental pollution control.

□ Degree/HNC □ High degree of practical skill and experience of classical analytical techniques □ Understanding of applications and limitations of modern instrumental methods □ Age under 27 □ Appointment as Scientific Officer (£1,318-£2,177) □ Ref: SA/4/MF □ Closing date 7 September 1973.

□ Application forms from Department of Trade and Industry, Warren Spring Laboratory, PO Box 20, Gunnels Wood Road, Stevenage, Herts SG1 2BX.

British Museum (Natural History) Department of Palaeontology

Palaeobotanical Technologist

■ Electron microscopy and plant histology and cytochemistry ■ For investigation of evolutionary development of pteridophytes and gymnosperms.

□ Degree, HNC or equivalent, preferably in Botany □ Experience in above fields essential □ Age under 30 □ Appointment as Scientific Officer (£1,493-£2,352) or Higher Scientiffic Officer (£2,251-£2,842) according to age, qualifications and experience □ Ref: SB/7/DK □ Closing date 7 September 1973.

□ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Science group. CIVIL SERVICE

UNIVERSITY OF LEICESTER

Applications are invited for three

Research Assistants

to join the X-ray Astronomy Group to participate in current space experiments. The Group is engaged in research in solar and cosmic physics using satellite and rocket-borne experiments which are designed and built by the Group. Also, there are active observing programmes using existing equipment on the SKYLAB and COPERNICUS satellites.

i) A physicist/astronomer is required to work in solar physics research, who will be primarily responsible for analysis and interpretation of data from the coordinated rocket/Skylab solar observing programme. Postgraduate experience is desirable in solar or relevant atomic physics and computing experience would be of value.

ii) An applied scientist is required to work on the design and development and to be responsible for the production of soft X-ray detection systems using proportional counters. Postgraduate experience is desirable in radiation detection techniques or gas discharge physics, and awareness of the technology of space instrumentation, hardware and electronics could be useful.

iii) A mathematician or physicist is required to work on the interpretation of data from satellite experiments which are designed to study cosmic X-ray sources, who will be responsible for developing computer software for the reduction and analysis of experimental data and will participate in the planning of observing programmes. Postgraduate experience in high energy astrophysics and/or computing is desirable.

Appointments will be from October 1973 until December 1975, in the first instance. Salaries will be on the Lecturer scale in the range £1929–£2533 p.a. depending on qualifications and relevant experience.

Applicants should write to: **Dr K. A. Pounds, Department of Physics, University of Leicester,** before 31 August 1973, giving details of qualifications and relevant experience.

(295)

Technical Editor

The Royal Dutch/Shell Group require, at their research centre in Amsterdam, a technical editor for scientific and technical reports and publications. His responsibilities will comprise liaison with authors, typists and illustrators.

We expect the post to be filled by an engineering or a science graduate with a good command of English, but candidates with other, equivalent, qualifications will also be considered. Experience will be an obvious advantage.

Travelling and other reasonable expenses will be paid for interviews in London and Amsterdam. We will give financial assistance with the removal of household effects to Holland.

Applications, giving full details of qualifications and experience, should be sent to:

SHELL INTERNATIONAL PETROLEUM COMPANY Ltd.,
Recruitment Division (PNEL/1)

Shell Centre, London SE 1.

(258)

UNIVERSITY COLLEGE
GALWAY

PROFESSORSHIP OF PHARMACOLOGY

(within the Department of Experimental Medicine and Practical Pharmacology)

Applications are invited for the above statutory, whole-time post. Salary scale £4,827 by £123 (8) to £5,811, plus Family Allowances. Non-contributory Pension Scheme.

The closing date for receipt of applications is October 1, 1973. Prior to application, further information should be obtained from the Registrar of the College. (X80)

AGRICULTURAL RESEARCH COUNCIL

FOOD RESEARCH INSTITUTE
NORWICH

Higher Scientific Officer/Senior Scientific Officer

CHEMIST

Applications are invited for an appointment in the Chemistry Division to lead a small group concerned with metabolic studies on sprout suppressants. Experience in chemistry with a biological background, preferably with some analytical or radiochemical expertise, is desirable. A Ph.D. or equivalent experience is required.

Salary (with annual increments and F.S.S.U. superannuation) will be either HSO £2,076-£2,667 or SSO £2,615-£3,640 according to age and experience.

Closing date for applications is four weeks after the appearance of this advertisement.

Further details and application forms from: The Secretary, Food Research Institute, Colney Lane, Norwich NOR 7OF, quoting Ref. No. 73/9. (313)

UNIVERSITY COLLEGE, DUBLIN

DEPARTMENT OF AGRICULTURAL BIOLOGY

Applications are invited for the following two posts in the Department of Agricultural Biology :

ASSISTANT OR ASSISTANT LECTURER IN PLANT PATHOLOGY

Candidates should have a postgraduate degree in Plant Pathology, teaching experience and preferably (but not exclusively) research interests and training in one of the following areas: cytochemistry, plant ultrastructure, virology or bacteriology.

ASSISTANT OR ASSISTANT LECTURER IN FOREST OR HORTICULTURAL BOTANY

Candidates should have a post-graduate degree in Forest or Horticultural Botany, teaching experience and preferably (but not exclusively) research interests and training in Plant Physiology or Ecology.

The successful candidates will engage in teaching and research.

Salary scale will be in the range :
Assistant : £1,911×97—£2,105 ;
Assistant Lecturer : £2,195×122—£3,049.

A non-contributory pension scheme and family allowance (£107 in respect of wife and £75 in respect of each child under 18 years) are additional to salary.

Applicants should submit a curriculum vitae (three copies) together with the names of at least three referees (preferably persons with a knowledge of the applicant's qualifications and experience) to Mr J. P. MacHale, Secretary and Bursar, University College, Belfield, Dublin 4, from whom further particulars may be obtained, not later than August 30, 1973. (315)

M.R.C. CLINICAL RESEARCH CENTRE

(NORTHWICK PARK HOSPITAL)
WATFORD ROAD, HARROW,
MIDDLESEX HA1 3UJ

There is a vacancy for a GRADUATE (Honours degree essential) in biochemistry/microbiology for research involving gas chromatography of bacteria and products of bacterial metabolism. Knowledge of bacterial metabolism is essential; experience of gas chromatography is desirable not but essential. The appointment is for 3-5 years, and the salary, which is dependent upon age and experience, will be within the range £1,668 to £3,192 plus £162 London Allowance a year.

Further particulars and application forms may be obtained from Mrs. J. Tucker-Bull. Closing date September 7. Please quote Reference 116/1. (241)

SCIENTISTS

for forensic science laboratories

Forensic science laboratories provide scientific aid to the police in the investigation of crime and to the courts in the administration of justice.

Scientists joining the laboratories initially assist experienced forensic scientists. The work may involve visiting the scene of a crime, preparing reports and statements of evidence and appearing in court.

Metropolitan Police

Chemists

To fill a number of posts, in the General Chemistry section of the Metropolitan Police Forensic Science Laboratory in Central London. The work calls for the examination of a wide range of materials occurring both as traces, transferred between the criminal and the scene of the crime, and in many situations in relation to criminal offences. There may be a requirement to give evidence in court. Practical experience would be advantageous either of analysis or as a specialist, in one of the following: gas chromatography, X-ray defraction, or emission spectrography.

For details of salary and address for application form see panel below.

Home Office

There are vacancies for the following scientists in laboratories throughout the country.

Chemists

The work of Chemists covers a wide field of scientific enquiry, involving materials such as body fluids and tissues, drugs, explosives, glass, paints, metals, plastics, pesticides and soils. The most modern chemical and physical methods of analysis are used, for instance, atomic absorption spectrometry, scanning electron microscope with X-ray micro-analysis, and spectrofluorimetry. Reference: SB/2/LA.

Biologists

Biologists examine a great range of materials, including body fluids, hairs, fibres, and plant and animal material. Up-to-date specialised serological and analytical techniques are employed. Reference: SB/1/LA.

Physicists/Chemists

To examine documents for evidence on handwriting inks, paper, typescript and to decipher erasures and indented handwriting. Extensive photographic experience is required for one post: Reference: SB/5/LA.

Firearms Specialist

The work includes examining and testing firearms and ammunition, propellant powders and residues; evaluating gunshot damage and injuries. Photographic techniques, velocity measurements and other methods of investigation are used. A wide knowledge of firearms is essential. Reference: SB/3/LA.

Metallurgist

To examine items and evaluate accident damage to vehicles. He will also be concerned with counterfeit coins and metals. Reference: SB/6/LA.

Radio Immuno-Chemist

To develop work on the use of radioimmunoassay methods, especially applied to the detection of drugs in body fluids. Experience in the field, together with ability to work as a member of a small team is essential. Reference: SB/4/LA.

Appointments for all vacancies will be at either Senior Scientific Officer, Higher Scientific Officer or Scientific Officer level, depending on age, qualifications and experience.

A degree, HNC or equivalent in an appropriate subject is essential. For SSO, 1st or 2nd honours degree or equivalent is necessary, with at least four years' postgraduate experience, and age under 32. At least two years' postgraduate experience is needed for HSO, and age under 30. For SO age must be under 27. Salary ranges are, according to age and experience, SSO, £2615–£3640; HSO, £2076–£2667; SO, £1318–£2177. There is an additional London weighting of £175 for the Metropolitan Police Forensic Science Laboratory posts.

For the Metropolitan Police appointments and an application form (to be returned by 7 September), write to The Secretary, Room 733 (Chem), New Scotland Yard, Broadway, London SW1H 0BG. Please quote SA/2/DS.

For full details of the Home Office appointments and an application form (to be returned by 7 September), write to the Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone BASINGSTOKE 29222 ext 500 or LONDON 01-839 1992 (24 hour answering service), please quote appropriate reference.

(348)

UNIVERSITY OF LONDON

THE MIDDLESEX HOSPITAL MEDICAL SCHOOL

A vacancy exists from October 1, 1973, for a GRADUATE to assist with research on the problems of inflammation and rheumatoid arthritis. Opportunity to work for Ph.D. will be available for suitable appointee. Salary according to qualifications and experience within the range £1,227 to £1,461.

Applications including curriculum vitae and the names and addresses of two referees to Dr V. Eisen, Department of Rheumatology Research, The Middlesex Hospital Medical School, London W1P 9PG, by September 14, 1973. (269)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS AL5 2JQ

The Soil Survey of England and Wales (Swansea Centre) has a vacancy for a SCIENTIFIC OFFICER to map soils and study their distribution. Minimum qualifications are a pass degree in chemistry, physics, or the environmental sciences, or an equivalent qualification. Starting salary in scale £1,318 to £2,177. Superannuation with allowance on off-set contributions.

Applications, naming two referees and quoting reference 1952 to The Secretary by September 6.

(272)

THE ROYAL VETERINARY COLLEGE

DEPARTMENT OF ANATOMY

RESEARCH ASSOCIATE

Honours graduate with postgraduate experience in electron microscopy required for grant-supported (Agricultural Research Council) experimental studies of spermatogenesis in farm animals, commencing October 1, 1973. Salary according to age and experience.

Applications should be made before **August 31, 1973,** to The Secretary (N), The Royal Veterinary College, Royal College Street, London NW1 0TU, from whom further particulars may be obtained.

(270)

Head of Drug Safety Evaluation

Upon the appointment of the present holder to a University post, a vacancy exists for the position of Head of Drug Safety Evaluation at the Institute of Medical Research of John Wyeth & Brother, Taplow, Maidenhead, Berkshire.

Ideally, the candidate will have experience of those branches of toxicology necessary to validate the safety of any new drug for clinical study in man. The function of the post, however, will not be solely that of a routine toxicologist.

A qualification in or experience of pathology will be an added recommendation but this is not regarded as an essential feature of the appointment. Biochemical knowledge or experience in metabolic work would likewise be advantageous.

The successful applicant will work closely with colleagues in chemistry, pharmacology, pharmacy and medicine and play an integral role in all the appropriate aspects of modern medicinal research.

The salary associated with this appointment will be commensurate with the responsibilities of the post. Fringe benefits include a non-contributory pension and life assurance scheme. Assistance will be given towards the expenses incurred in relocation.

Please write in the first instance giving brief details of experience and qualifications to:

Cameron Wolstenholme, Personnel Controller,
John Wyeth & Brother Limited,
Huntercombe Lane South,
Taplow, Maidenhead, Berks, SL6 0PH.

Wyeth

(331)

HAILE SELLASSIE I UNIVERSITY—ETHIOPIA

Applications are invited for the post of

DIRECTOR OF INSTITUTE OF PATHOBIOLOGY

Applicants must be: a senior and experienced person at a level of Professor or Associate Professor, with broad interest in the promotion and utilization of science and technology for development ; preferably a person with first hand experience of work in developing countries or with a good knowledge and appreciation of the problems of developing countries such as Ethiopia ; a person with genuine interest to work with local experts and preferably a person with good international connections with potential donors (research grants) ; teaching duties will also be included in his role and therefore considerable teaching experience would be an advantage ; a person with extensive experience in research administration and a strong desire to work in a developing country ; a person with biological background and active research interest, in addition to adequate experience and qualifications, will be preferred but the field of specialization may not necessarily be a limiting factor.

Duties of appointee will include: directing and developing the Institute of Pathobiology within the frame-work of the Institute's Charter and the overall national priorities and needs in applied Biological Sciences in the broad sense ; providing the necessary guidance and actively undertaking the integration of the activities of the Institute with that of the Materials Research Unit and other units in the Faculties of Science and Technology into the proposed Institute for Scientific and Technological Research and Deevlopment (ISTRAD) ; critically evaluating the proposed charter for ISTRAD, improving where necessary, and developing, in collaboration with all concerned, a five and ten year project for the development of the new Institute ; developing an appropriate work Technological Research and Development (ISTRAD) ; critically evaluating the proposed charter helping to raise the necessary financial support from both local and international sources to develop ISTRAD, and to establish appropriate international contacts ; promoting the institutional objectives of ISTRAD, in institutionalizing contract research undertakings, advising on dual appointments between the Institute and other units of the University and creating the necessary machinery to run the Institute on a semi-autonomous basis, primarily supported by contract funds and research grants ; promoting the educational objectives of ISTRAD by encouraging research by both staff and students of different faculties as well as by encouraging ISTRAD staff to teach in different faculties of the University ; serving as a consultant and promoter of the Ethiopian Science Foundation and the National Council for Science and Technology.

Salary scale: Professor Eth.$16,800-Eth.$21,600 p.a. Associate Professor Eth.$13,200-Eth.$18,000 p.a. (£1 sterling=Eth.$5.5 approximately.) Salary may be supplemented in range £1,050-£1,200 p.a. (sterling—normally free of all tax) and children's education allowances and holiday visit passages may also be provided. The appointment will be for 2 years in the first instance, renewable. In addition, 10% gratuity, in lieu of superannuation, on salary supplementation and an appointment grant.

Housing allowance. Family passages and baggage allowance.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by airmail, not later than September 13, 1973, to the Office of the Associate Academic Vice President for Staff Affairs, Haile Sellassie I University, P.O. Box 1176, Addis Ababa, Ethiopia. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (325)

UNIVERSITY OF EDINBURGH

DEPARTMENT OF BIOCHEMISTRY

LECTURER

Applications are invited for the post of Lecturer in this Department which is housed in the Medical School. The lecturer appointed will be expected to participate in teaching to medical, dental or science students, and to take an active part in research. Initial salary will be in the range £1,929 to £4,548 with superannuation provision under F.S.S.U.

Further particulars may be obtained from the Secretary to the University, Old College, South Bridge, Edinburgh EH8 9YL, with whom applications (6 copies), together with the names of two referees, should be lodged by September 15, 1973. Please quote reference 1057.

(291)

NEW ZEALAND

MINISTRY OF AGRICULTURE & FISHERIES

Applications are invited for the undermentioned vacancy.

SCIENTIST

WHATAWHATA HILL COUNTRY RESEARCH STATION, HAMILTON

Salary: Up to $NZ10,577 depending on qualifications and experience.

Duties: Studies in the reproductive physiology of sheep and beef cattle with particular reference to the influence of nutritional and management factors affecting the fertility of hill country flocks and herds. Large numbers of genetically different sheep and cattle are available for study.

Qualifications desired: Masters or higher degree in Agricultural or Veterinary Science, preferably with research experience in the general field of reproductive physiology.

Passages: Fares for appointee and if married, his wife and family will be paid.

Incidental expenses: Up to £55 for a single man and £183 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and general information are available from the High Commissioner for New Zealand, New Zealand House, Haymarket, London SW1Y 4TQ, with whom applications will close on September 28, 1973.

Please quote reference B13/2/202/3548 when enquiring. (278)

UNIVERSITY COLLEGE OF NORTH WALES

BANGOR

GRADUATE FOR TECHNICAL RESEARCH

This post, available for two years in the first instance, offers a graduate or Ph.D. broad experience in physico-chemical instrumentation, with special reference to microwave spectroscopy and double-resonance, and participation in new studies of molecular structure. Day-to-day responsibility for running of instruments is included, but the appointee would be expected to contribute to the scientific programme, and publications. The group, under Professor J. Sheridan, includes two lecturers and two research fellows, and would provide a climate of expert knowledge for a candidate without microwave experience. There are excellent back-up facilities in electronics and mechanical work, in a modern laboratory. Experience related to spectroscopy and some knowledge of electronics would be an advantage.

Salary (under review): £1,881 by £72 to £1,953 per annum.

Applications (two copies), giving full details of age, qualifications and experience together with the names and addresses of two referees should be submitted to the Secretary and Registrar, University College of North Wales, Bangor, by not later than September 30, 1973. (279)

UNIVERSITY OF NAIROBI

KENYA

Applications are invited for **SENIOR LECTURESHIP IN PLANT ECOLOGY** in Department of Applied Plant Sciences. Applicants can be graduates in Botany or Biology who hold a Ph.D. in either Plant Ecology or Range Ecology. Experience in teaching and in ecology of tropical rangelands would be an advantage. Salary scale: K£2,256 to K£3,036 per annum (K£1=£1.14 sterling). The British Government may supplement salary by £950 per annum (sterling) for married appointee or £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. F.S.S.U. Family passages; various allowances.

Detailed applications (2 copies) including curriculum vitae and naming 3 referees, should be sent by air mail, not later than September 12, 1973, to the Registrar, University of Nairobi, P.O. Box 30197, Nairobi, Kenya. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of the appointment may be obtained from either address. (263)

PHYSIOLOGIST—ENDOCRINOLOGIST

A physiologist-endocrinologist whose primary species responsibility is poultry but who has a broad interest in animal agriculture including swine and ruminants. Emphasis is to centre on female reproduction and behaviour. Responsibilities of this position include research, teaching and extension. Appointment at the rank of Assistant or Associate Professor.

Applicants should write to: W. D. Morrison, Professor and Chairman, Department of Animal and Poultry Science, Ontario Agriculture College, University of Guelph, Guelph, Ontario, Canada N1G 2W1. (276)

UNIVERSITY OF THE WEST INDIES

JAMAICA

Applications are invited for post of (a) **SENIOR RESEARCH FELLOW** or (b) **RESEARCH FELLOW IN THE FAMILY PLANNING PROGRAMME OF THE DEPARTMENT OF SOCIAL AND PREVENTIVE MEDICINE.** The appointment is for one year. Appointee will be a member of a team involved in research and training in family planning and population dynamics, action oriented, and functioning in collaboration with the National Family Planning Board and other appropriate University Departments. Appointee should have expertise and experience in Statistics, Data Processing, Sociology/Demography, Sampling Procedures and Research Methodology. Salary scales: (a) £2,700 to £4,200 per annum; (b) £1,850 to £3,265 per annum. Child allowance. F.S.S.U. Under the terms of the funding of this programme, passages are not paid from overseas.

Detailed applications (3 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail, as soon as possible to the Registrar, University of the West Indies, Mona, Kingston 7, Jamaica. Further particulars are available similarly and should be obtained before an application is made. (264)

UNIVERSITY OF THE SOUTH PACIFIC

FIJI

Applications are invited for post of (a) **CHIEF TECHNICIAN** or (b) **SENIOR TECHNICIAN IN CHEMISTRY** in the School of Natural Resources, tenable from January 1974. Applicants should possess the Advanced Certificate in Laboratory Technology of the City and Guilds of London Institute, H.N.C. or equivalent and have several years' experience in a Chemistry teaching laboratory. Familiarity with Organic and Physical Chemistry undergraduate laboratories is highly desirable and proficiency in related fields such as glass-blowing, instrumentation, first aid or safety would be an advantage. Appointee will be responsible for the supervision of technicians and technical assistants who are engaged in the preparation and the running of the Chemistry Laboratories at the research, degree, preliminary and diploma levels under the overall control of the Laboratory Manager and for the operation of these laboratories in accordance with the requirements of the chemistry staff. The work will involve the training of junior staff; the maintenance of laboratory equipment and instrumentation; the ordering and stock-keeping of chemicals and glassware. Salary scales: (a) $F3,900 to $F5,900 per annum; (b) $F2,700 to $F3,700 per annum (£1 sterling=$F1.98).

Details of form of application, further particulars and outline terms of service are obtainable from The Registrar (Post 73/33), University of the South Pacific, P.O. Box 1168, Suva, Fiji, to whom completed applications should be returned by September 13, 1973. (265)

UNIVERSITY OF NAIROBI

KENYA

Applications are invited for **LECTURESHIP IN DEPARTMENT OF ANIMAL PHYSIOLOGY.** Applicants should hold a Veterinary or Medical degree with a Ph.D. in some aspects of Mammalian Physiology. Alternatively, they may possess an Honours degree in Physiology with a higher degree in Mammalian Physiology, preferably Reproductive Physiology and Endocrinology. Salary scale: K1,500-K£2,580 p.a. (K£1=£1.16 sterling). The British Government may supplement salaries in range £450-£750 p.a. (sterling) if married, or £150-£450 p.a. (sterling) if single, normally free of all tax. F.S.S.U. Family passages; various allowances.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail not later than September 17, 1973, to the Registrar, University of Nairobi, P.O. Box 30197, Nairobi, Kenya. Applicants resident in U.K. should also send 1 copy to the Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of this appointment may be obtained from either address. (321)

The Company of People

STERLING-WINTHROP
GROUP

Chief Microbiologist

Winthrop Laboratories is a major pharmaceutical company in the U.K. and through its production division manufactures ethical and proprietary products for many countries throughout the world.

We wish to appoint a Chief Microbiologist who will assume responsibility for managing the microbiology laboratory, presently staffed by four graduate microbiologists and four technicians.

The work carried out by the laboratory covers most aspects of industrial microbiology. This includes sterility testing of a range of sterile products, control of proprietary products and raw materials. Antibiotic and vitamin assays. Development work on new products, in process controls in the sterile products department, and 'trouble shooting' in the production departments.

The person appointed will have a formal education to degree level in microbiology together with several years industrial experience, preferably in the pharmaceutical industry. An awareness of current medicines legislation is necessary together with the ability to implement changes through the principles of management.

Salary and other conditions are those expected of an expanding International organisation.

Please write or telephone for an application form.

Miss Susan G. Shaw, Personnel Officer,
Winthrop Laboratories Production Division,
Fawdon, Newcastle upon Tyne NE3 3TT.
Telephone: Gosforth Northumberland 853931.

WINTHROP
WINTHROP LABORATORIES (287)

KING'S COLLEGE HOSPITAL GROUP have a vacancy in the Division of Pathology for a **SENIOR TECHNICIAN** to organize diagnostic immunology within a research laboratory. The work will include the use of standard immunology techniques and the development of new methods. Salary and conditions according to Whitley Council agreement for Medical Laboratory Technicians.—Applications should be sent immediately to: The Principal Technician, Division of Pathology, King's College Hospital, Denmark Hill, London, S.E.5. (349)

MEDICAL RESEARCH COUNCIL UNIT requires two **JUNIOR TECHNICAL OFFICERS**, one to assist with research involving tissue culture, and the other with the preparation of histological material. Experience desirable for the latter post, but not essential, since training can be provided. Salaries in accordance with qualifications and experience.—Apply to The Director, M.R.C. Experimental Radiopathology Unit, Hammersmith Hospital, London W12 0HS. (273)

THE NATIONAL RADIOLOGICAL PROTECTION BOARD HARWELL

are seeking

SCIENTISTS

to fill vacancies in the

BIOLOGY DEPARTMENT

of the

RESEARCH & DEVELOPMENT DIVISION

The research programme includes studies of the metabolism of higher actinides, their removal from body tissues and their interaction with biological materials in cellular systems.

The posts, which are at the Board's Headquarters at Harwell, would be of interest to scientists trained in one of the biological sciences: previous experience of the chemistry of actinides is not essential. Applicants should have a first or good Second Class Honours degree.

Appointment will be in the grade of Scientific Officer or Higher Scientific Officer depending upon the level of qualification and experience. The salary scales appropriate to these appointments are:

Scientific Officer:	£1,415–£2,330 per annum.
Higher Scientific Officer:	£2,225–£2,855 per annum.

For further information and an application form write or telephone:

Personnel Officer (Ref. A.37),
National Radiological Protection Board,
Harwell, Didcot, Berks.
Telephone: Rowstock 600 (STD Code 023-583), Extn. 33.

Closing date for receipt of application forms: Friday, September 7, 1973.

(292)

Pathologist

Our Toxicology Unit is expanding into new purpose-built laboratories and we require a pathologist to assist in the safety assessment of new pharmaceutical compounds.

Duties will include the interpretation of histo-pathology, routine and specialized clinical examinations of experimental animals. Experience in these areas is therefore desirable but training will be given where necessary. In any event, the post offers an excellent opportunity to become familiar with many aspects of laboratory animal pathology.

Candidates should preferably possess a degree in veterinary science or a relevant Biological discipline.

A competitive salary will be paid and there are the usual benefits which one associates with a large, British-based company. The Medicinal Research Centre is located one mile from Harlow New Town and combines easy access to London with proximity to pleasant countryside.

If you would like to be considered for this post, please write, outlining your career to date, to:

BRL

John Atkinson, Personnel Officer,
Beecham Research Laboratories,
Fourth Avenue, The Pinnacles,
Harlow, Essex.

1972

(289)

KINGSTON POLYTECHNIC SCHOOL OF GEOLOGY

RESEARCH ASSISTANT

in the field of
PALAEOZOOLOGY-PALAEOECOLOGY OF VERTEBRATES

to start as soon as possible.

If appointed, you will undertake research in various aspects of the distribution and palaeoecology of the vertebrate faunas of the Lower Eocene deposits of Europe and North Africa under the supervision of Dr R. T. J. Moody. You will be expected to register for a higher degree.

Starting salary £1,320 per annum.

Further particulars and application forms (to be returned as soon as possible) from Appointments Officer, Kingston Polytechnic, Penrhyn Road, Kingston upon Thames KT1 2EE, 01-549 1366. (271)

AUSTRALIAN NATIONAL UNIVERSITY

WARDEN—GARRAN HALL

Applications are invited from suitably qualified men and women for appointment to the position of Warden, in a University Hall of Residence, accommodating 250 students (men and women).

The University wishes to maintain flexibility in the conditions of appointment offered for the position. Primarily it wishes to appoint a Warden who can participate in teaching and/or research in the University. It will consider applications from suitably qualified persons willing to occupy a wardenship for a limited period, and from persons interested in a longer tenure of office (it is not envisaged that appointment will be for less than three years) and will be willing to offer a continuing appointment in an appropriate academic department.

Salary will be equivalent to that of Reader, $A15,940 per annum, and there is an entertainment allowance of $A400 per annum.

Rent free accommodation will be provided.

Further information may be obtained from the Registrar, P.O. Box 4, Canberra ACT 2600, Australia, to whom applications, quoting the names and addresses of three referees, should be forwarded by September 24, 1973, or from the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF. (299)

UNIVERSITY OF ADELAIDE

Applications are invited for the following appointments :

SENIOR DEMONSTRATOR IN PHYSICS from 1974. Duties will include undergraduate laboratory teaching and responsibility for operation of one of the undergraduate laboratories, including supervision of laboratory staff, training of part-time demonstrators and assistance with design and construction of new experiments. Participation in research programmes will also be encouraged. (21.9.73)

SENIOR LECTURER IN ANATOMY AND HISTOLOGY. Registrable medical qualifications desirable but not essential. The Department teaches students of medicine, dentistry, science, physiotherapy and occupational therapy. Research fields are neuroendocrinology (using electrophysiological and electron microscopic techniques), human and comparative neurology, cell biology (including cytochemistry), experimental embryology and clinical anatomy. (28.9.73)

Salary scales: Senior Lecturer $A12,268—408(5)—$A14,308 ; Tutor/Demonstrator $A5,332—408(1)—255(5)—$A7,015 ; with superannuation on the F.S.S.U. basis. Tutor/Demonstrator appointments are non-tenured and non-superannuated. In the Faculty of Medicine special additional allowances are payable for medical qualifications registrable in South Australia (currently under review).

Further particulars about these posts and the conditions of appointment and other information sought will be supplied on request to the Registrar of the University, or to the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PT. (Tel.: 01-387 8572).

Applications should be sent in duplicate and giving the information listed in the Statement that will be supplied, to the Registrar, the University of Adelaide, North Terrace, Adelaide, South Australia 5001.

(334)

BIRKBECK COLLEGE

(UNIVERSITY OF LONDON)

DEPARTMENT OF GEOLOGY

RESEARCH ASSISTANT

Applications are invited from honours graduates in Geology with experience of analytical geochemistry. Knowledge of X-ray diffraction techniques would be an advantage. The research will be mainly concerned with geochemical and other studies of rocks and minerals from the Lizard peninsula, Cornwall.

Appointment for two years in the first instance, with the possibility of an extension for a further year. Salary in the range £1,497 to £2,223.

Applicants should write to the Deputy Secretary (N), Birkbeck College, Malet Street, London WC1E 7HX, giving details of age, qualifications and experience, with the names of two referees, by August 24, 1973. (286)

UNIVERSITY OF DUNDEE

DEPARTMENT OF BIOLOGICAL SCIENCES

Applications are invited from graduates in Botany, Agriculture or a related subject, for an Agricultural Research Council Research Assistantship to work on the effects of shading on nitrogen fixation in legumes. Salary dependent on qualifications but probably around £1,400 per annum.

Applications (including the names and addresses of 2 referees) should be sent as soon as possible to Dr J. I. Sprent, Department of Biological Sciences, The University, Dundee DD1 4HN, from whom further information can be obtained. Please quote reference Est/62/73J. (346)

UNIVERSITY OF TASMANIA

Applications are invited for the following posts:

LECTURER IN ANATOMY. Applicants should have experience in anatomical teaching and research. A medically qualified appointee will receive a loading of $A630 per annum additional to the salary quoted below.

LECTURER IN CIVIL ENGINEERING. The appointee will be able to choose his own special field of interest in addition to taking part in the general teaching of the department, which covers the whole field of Civil Engineering.

LECTURER IN ELECTRICAL ENGINEERING. Applicants should hold a Ph.D. degree or equivalent qualifications, taking into account any industrial experience. They should preferably have active research interests. Preference will be given to applicants whose main field of interest is either communications electronics, or electrical power engineering, or control engineering. However, applicants with any field of interest in electrical engineering will be fully considered.

LECTURERS IN GEOGRAPHY (two posts). Applications are invited from specialists in one or more of the following fields: spatial analysis, climatology, soil geography, agricultural geography, urban and regional analysis.

LECTURER IN MECHANICAL ENGINEERING. Preference will be given to an applicant with some experience in machine design or in vibrations.

The current salary scales are:

Senior Lecturer: $A12,268-$A14,308
Lecturer Grade I: $A10,575-$A11,982
Lecturer Grade II: $A8,698-$A10,106
Senior Tutor Grade II: $A7,270-$A8,698
Tutor: $A5,740-$A7,015.

Appointments will be offered within one of these grades according to qualifications and experience.

Application forms and further particulars obtainable from the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications close September 12, 1973. (332)

QUEEN MARY COLLEGE

(University of London)

DEPARTMENT OF ZOOLOGY AND COMPARATIVE PHYSIOLOGY

Applications are invited for the post of RESEARCH TECHNICIAN (grade 3) to work in the field of insect neurophysiology on a project involving the structural and functional organisation of neural pathways in insect photoreceptors. Applicants should have some knowledge of electrophysiological techniques and/or histology and fluorescence microscopy. The appointment will be for approximately two years. Salary £1,539 per annum plus London Weighting £175 per annum. Five day week, five weeks (in total) annual leave.

Letters only to Assistant Secretary (Establishment) (N), Queen Mary College, Mile End Road, London E1 4NS, stating age, experience, qualifications and present work. Closing date August 31. (336)

UNIVERSITY OF IFE

NIGERIA

Applications are invited for LECTURESHIPS IN DEPARTMENT OF CHEMISTRY, tenable as soon as possible. Applicants must have teaching and practical experience in Organic, Inorganic, Analytical and Physical Chemistry. They must either hold a Ph.D. or be about to receive it. Duties of appointee include both teaching and research. Salary scale: N2,760-N4,830 p.a. (£1 sterling=N1.62). The British Expatriates Supplementation Scheme is unlikely to be applied to these appointments. Family passages; superannuation and medical schemes; various allowances; regular overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail, not later than September 17, 1973, to the Registrar, University of Ife, Ile-Ife, Nigeria. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, W1P 0DT. Further particulars of the appointment may be obtained from either address (324)

UNIVERSITY OF WALES

University College of Swansea

DEPARTMENT OF CHEMISTRY

Applications are invited for vacancies of RESEARCH DEMONSTRATOR in the Department of Chemistry. Applicants in all branches of Chemistry will be considered but candidates should hold, or expect to receive a Ph.D. degree in the near future. Those appointed will be expected to participate in one of the numerous research programmes in the department.

The posts, which are tenable from October 1, 1973, will be for one year in the first instance. The salary will be in the scale £1,584-£1,665 per annum together with F.S.S.U. benefits.

The closing date is Friday, August 31.

POSTDOCTORAL RESEARCH ASSISTANTS

Applications are invited for three vacancies of POSTDOCTORAL RESEARCH ASSISTANTS in the Department of Chemistry, to work on the following S.R.C. sponsored projects.

Physical Chemistry

(a) Infra-red cryogenic/photolytic studies (Dr. H. E. Hallam) and

(b) a novel free-radical buffer technique for the study of alkyl radical (gas phase recombination rates) (Dr. R. M. Marshall).

Organic Chemistry

(c) Study of the mechanism of 1,2-aryl migrations involving spirodienone intermediates (Dr. R. S. Ward).

Candidates should have, or expect to receive in the near future, a Ph.D. degree. For project (a) above, preference will be given to those with experience in photochemistry or vibrational spectroscopy.

The posts are tenable from October 1, 1973, and will be for one year in the first instance, at a salary of £1,764 per annum.

The closing date is Friday, August 31.

DEPARTMENT OF ZOOLOGY

Applications are invited for a vacancy of RESEARCH ASSISTANT in the Department of Zoology to work on an S.R.C. supported project with Dr. N. A. Ratcliffe on the Cellular Aspects of insect immunity. The applicant should possess a good honours degree and competence in cell fractionation, immunology, tissue culture, microbiology or cell-cell interaction techniques.

The appointment, which will be for three years from October, 1973, will be on the scale £1,380-£1,590 per annum. However, if the successful candidate is allowed to read for a higher degree then the salary will be reduced to the net equivalent of an S.R.C. studentship.

The closing date is Friday, August 31.

Further particulars and application forms (2 copies) for these posts may be obtained from the Registrar/Secretary, University College of Swansea, Singleton Park, Swansea SA2 8PP, to whom they should be returned by the appropriate closing dates. (351)

Laboratory Animal Services

As an integral part of site expansion, we are currently developing our facilities for laboratory animals. New, purpose-built premises are being built and we require a man with sound experience to become responsible for these facilities.

He will be expected to lead a team of around 20 staff and must be capable of working with a minimum of supervision. The successful candidate is likely to be either a graduate in one of the Biological Sciences or an Associate of the Institute of Animal Technicology In any event, he must have had a good background in handling laboratory animals and be capable of liaising effectively with our research scientists.

Salary will be competitive and there are the usual fringe benefits which one associates with a large, British-based company. The Medicinal Research Centre is located one mile from the centre of Harlow New Town and combines easy access to both London and pleasant countryside.

If you would like to be considered for this post, please write, outlining your career to date, to:

BRL

John Atkinson, Personnel Officer,
Beecham Research Laboratories,
Fourth Avenue, The Pinnacles,
Harlow, Essex.

1972

(288)

Chemical Technical Assistant

Shell Research Limited, Sittingbourne, Kent, have a vacancy in the Metabolic and Environmental Chemistry Section of the Chemical Toxicology Division of their Tunstall Toxicological Laboratory for a young technical assistant to work on the analysis, mainly by chromatographic procedures, of a range of samples including animal tissues, birds' eggs etc., for a number of substances including organochlorine and organophosphorus pesticides. The development as well as the application of the necessary methods will be involved, and there will be some opportunity to take part in studies, involving radioisotopes, of the metabolism of foreign compounds in animals.

This post would suit someone who has studied chemistry up to HNC level or equivalent and who also has some experience in chromatographic techniques including gas-liquid chromatography. However, applicants who have recently left or are about to leave school and have studied chemistry up to at least A-level or equivalent will also be considered. The level of appointment will depend on background and experience, and the salary offered will be competitive.

Please write or telephone for an application form, addressing enquiries to Shell Research Limited, Personnel Division (N), Sittingbourne, Kent ME9 8AG. (Telephone: Sittingbourne 4444, Extension 203).

(262)

BRUNEL UNIVERSITY

Polymer Science and Technology

TECHNICIAN

required to be responsible for running laboratories used primarily for teaching polymer chemistry at undergraduate level.

Minimum qualifications required are an O.N.C. in Chemistry together with some experience of polymer science or technology. A knowledge of instrumental analysis or materials characteristics would be an advantage.

Salary in the Technician grade 4 scale £1,728 to £2,028 plus £90 London Weighting.

37½ hour week, 20 days' leave plus 1 week at Christmas and Easter.

Postcard for application form to Establishment Secretary, Brunel University, Uxbridge UB8 3PH (quoting reference PSc/7) or telephone Uxbridge 37188, extension 49. Closing date: August 31, 1973.

(352)

THE DISTILLERS COMPANY LIMITED

GENETICIST

Geneticist required for the laboratories of the Yeast and Food Division Research Department which are situated in a rural area about five miles from Stirling.

The applicant, a recently qualified B.Sc. or Ph.D., should have a thorough grounding in the fundamentals of microbial genetics. The work is mainly concerned with the development of industrially useful strains of yeast but some background work of a more fundamental nature would also be required.

Applications, together with detailed information regarding training and experience, should be made in the first instance to The Manager, The Distillers Company Limited, Glenochil Technical Centre, Menstrie, Clackmannanshire.

(358)

CHARING CROSS HOSPITAL MEDICAL SCHOOL

require TECHNICIAN/GRADUATE for Research Unit in the Department of Obstetrics, West London Hospital. Experience in Tissue Culture and/or Immunology desirable. Appointment for 1 year in the first instance. Salary, according to Whitley scales, in range £1,461 to £1,980.

Apply to Secretary, Charing Cross Hospital Medical School, Brandenburgh House, London W6 9HH.

(275)

UNIVERSITY OF CAPE TOWN

LECTURESHIP IN MATHEMATICS

Applications are invited for the post of Lecturer in Mathematics. The successful applicant will be expected to assume duties on February 1, 1974. This commencing date may be adjusted under special circumstances. The salary scale is R4,800×300—R6,900 per annum, plus a 15% pensionable allowance.

Applicants should state their age, experience and qualifications, publications and research interests, present salary, and should give the names and addresses of two referees, preferably persons with knowledge of the applicant's academic qualifications and experience, whom the University may consult.

Two copies of the application should reach the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF (from whom memoranda giving the conditions of service, including transport expenses on appointment, and information on the work of the Department may be obtained) not later than September 21, 1973. A third copy of the application should be sent direct by airmail to the Registrar, University of Cape Town, Private Bag, Rondebosch, Cape Town, South Africa, by the same date.

Appointment will be subject to a satisfactory medical certificate. The University reserves the right to appoint a person other than one of the applicants or to make no appointment.

(333)

UNIVERSITY OF IFE

NIGERIA

Applications are invited for posts of PROFESSOR, SENIOR LECTURER AND LECTURER IN DEPARTMENT OF PHYSICS. Interest and research experience in any of the following areas will be an advantage: Atomic and Molecular Spectroscopy; Solid State Theory, X-ray Crystallography and Solid State Spectroscopy; Environmental Physics (Atmospheric or Geophysical). Salary scales: Professor N6,600 p.a. Senior Lecturer N5,030-N5,750 p.a. Lecturer N2,760-N4,830 p.a. (£1 sterling=N1.62). The British Government may supplement salaries in range £750-£1,500 p.a. (sterling) for married appointee or £250-£1,000 p.a. (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. Family passages; superannuation and medical schemes; various allowances; regular overseas leaves.

Detailed applications (2 copies), including curriculum vitae and naming 3 referees, should be forwarded by airmail, not later than September 17, 1973, to the Registrar, University of Ife, Ile-Ife, Nigeria. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of the appointment may be obtained from either address.

(320)

UNIVERSITY OF ADELAIDE

Applications are invited for appointment as a

POSTDOCTORAL FELLOW IN ANIMAL PHYSIOLOGY

tenable in the Department of Animal Physiology at the Waite Agricultural Research Institute. The appointment, which is financed by a grant from the Reserve Bank is available for one year in the first instance, and renewable for a further year.

The work will involve studies on the endocrine background of functional efficiencies of animals. Experience with biochemistry, radioimmune assay and physiological genetics would be advantageous.

Salary scale: $A6,967+$A353(4)—$A8,379.

Applications, in duplicate, giving particulars of age, qualifications (including dates obtained), experience and the names and addresses of two referees, should be sent to reach the Registrar, The University of Adelaide, S. Australia 5001, not later than September 15, 1973.

(326)

UNIVERSITY OF MANCHESTER

RESEARCH ASSOCIATE IN HIGH ENERGY PHYSICS

Applications invited for this post from experimental physicists with a Ph.D. in High Energy Physics. The successful applicant would work in the Manchester group at present engaged in an experiment on the Intersecting Storage Rings at CERN, Geneva, using a magnet-spark chamber spectrometer to study particle production at small angles. He would be resident most of the time in Geneva. Salary per annum: £1,929 to £2,388. F.S.S.U.

Applicants should write to Professor P. G. Murphy, Physics Department, The University, Manchester M13 9PL, by September 15, 1973.

(296)

THE ANIMAL VIRUS RESEARCH INSTITUTE

Pirbright, Woking, Surrey

DEPARTMENT OF EXPERIMENTAL PATHOLOGY

Applications are invited for a post in the above Department. Applicants should have had experience in histological, histochemical and immunohistological procedures to provide support for a small group studying the pathogenesis of vesicular diseases in farm animals. Familiarity with the preparation of specimens for, and the use of, the electron microscope an advantage. The appointment will be in either the S.O. grade (£1,318-£2,177) or H.S.O. grade (£2,076-£2,667), depending on qualifications and experience. Minimum qualifications required, degree in scientific subject: I.M.L.T. ; H.N.C. ; H.N.D. or equivalent for appointment in S.O. grade ; similar qualifications required for appointment in H.S.O. grade with at least five years' appropriate scientific experience since qualifying ; applicants with first or second class honours degrees or equivalent should have had at least two years' postgraduate research experience. Superannuation Scheme with allowance to offset contributions. House available for suitable married applicant.

Further particulars and application forms from Secretary. (308)

UNIVERSITY OF MASSACHUSETTS

POLYMER ENGINEER

An important position in the School of Engineering at the University of Massachusetts, Amherst, has been made available. Applications will be welcome from candidates who are sufficiently qualified for a teaching position at the assistant or associate professor level, and whose research interests lie in the areas of polymer fabrication or macroscopic solid state properties. The successful candidate would be expected to work closely with the Polymer Science and Engineering Program and to initiate joint research projects. Applicants must have relevant experience in polymers and preferably teaching experience in Engineering.

Prospective applicants should submit their resumes to the Chairman of the Search Committee, Polymer Science and Engineering Program, University of Massachusetts, Amherst, Massachusetts 01002. We are an equal opportunity, affirmative action employer. (277)

NATIONAL MUSEUM OF WALES

APPOINTMENT OF ARCHAEOLOGICAL CONSERVATOR

Applications are invited from men or women for the new post of Archaeological Conservator (Research Assistant II) in the Department of Archaeology. The successful candidate will work in the existing departmental laboratory, which is shared with the Archaeological Conservator of the Council of Museums in Wales but will be responsible to the Keeper of Archaeology. Applicants should have an appropriate qualification in conservation, such as the University of London Diploma in Conservation and particular knowledge of casting techniques and pottery restoration would be an advantage.

Salary scale £1,384 to £2,286. Contributory superannuation. Generous leave.

Closing date for applications August 31, 1973. Full details from Secretary, National Museum of Wales, Cardiff CF1 3NP. (274)

UNIVERSITY OF LIVERPOOL

DEMONSTRATOR/SENIOR DEMONSTRATOR IN MICROBIOLOGY

Applications are invited for the post of Demonstrator/Senior Demonstrator in microbiology in the Department of Botany from candidates with postgraduate experience and interests in mycology or bacteriology.

The post is tenable from October 1, 1973, for one year in the first instance, renewable year by year, though not normally more than twice.

Salary scale £1,572 to £2,178 per annum together with F.S.S.U. benefits.

Applications, together with the names of three referees, should be received not later than August 24, 1973, by the Registrar, The University, P.O. Box 147, Liverpool L69 3BX, from whom further particulars may be obtained. Quote Ref. RV/N/80418. (257)

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

(UNIVERSITY OF LONDON)

Denmark Hill, London SE5 8RX

SENIOR TECHNICIAN with haematological experience, required to join multi-disciplinary group working on coagulation disturbance including the use of concentrates in liver disease. Salary £2,073. Further particulars from Dr Roger Williams, Liver Unit.

Applications, with the names of two referees, to the Secretary (N), not later than August 31, 1973. (303)

GESELLSCHAFT FÜR KERNFORSCHUNG M.B.H. KARLSRUHE

Für das im Kernforschungzentrum Karlsruhe gelegene

Institut fur Reaktorbauelemente

wird ein Nachfolger für den aus Altersgründen ausscheidenden

INSTITUTSLEITER

gesucht. Der fachliche Schwerpunkt des Instituts liegt auf den Gebieten

Angewandte Thermodynamik und Thermohydraulik

Gemeinsam mit anderen Instituten des Kernforschungszentrums werden zur Zeit vor allem Arbeiten im Zusammenhang mit reaktortechnischen Projekten durchgeführt. Der neue Institutsleiter sollte als anerkannter Wissenschaftler im Bereich der genannten Fachgebiete ausgewiesen sein und die Fähigkeit besitzen ein Team erfahrener Mitabeiter zu führen, die laufenden Vorhaben gezielt fortzusetzen und neue Aufgaben anzuregen. Die Ausstattung des Kernforschungszentrums gewährleistet hervorragende Arbeitsmöglichkeiten. Eine Zusammenarbeit mit der nur wenige Kilometer entfernten Universität Karlsruhe sowie den anderen benachbarten Universitäten ist wünschenswert und in verschiedenen Bereichen des Kernforschungszentrums institutionalisiert.

Richten Sie bitte Ihre Bewerbung bis 5.9.1973 mit Lebenslauf, Lichtbild, Zeugnissen und Veröffentlichungsliste an die Geschäftsführung der Gesellschaft für Kernforschung m.b.h., 75 Karlsruhe, Postfach 3640.

(355)

BACTERIOLOGIST

Quality Control

An expanding firm of pharmaceutical manufacturers wish to recruit a graduate—or other suitably qualified—bacteriologist for monitoring and control of products and environment. Experience of control work in the pharmaceutical or a comparable industry is essential.

Our factory is pleasantly situated on the outskirts of Huddersfield and help with re-location will be given for both these appointments. Salary is negotiable probably from £2,000.

Apply in confidence with career details to:

R. Thornton
Managing Director
Thornton & Ross Ltd
Linthwaite Laboratories
Huddersfield
Tel: Slaithwaite 2217

(347)

UNIVERSITY OF SUSSEX

SCHOOL OF BIOLOGICAL SCIENCES

RESEARCH ASSISTANT

Applications are invited for the post of Research Assistant to work on the biochemistry and cytochemistry of salt tolerance in plants. The work which will be for three years under the supervision of Drs T. J. Flowers and J. L. Hall, is financed by a grant from the Nuffield Foundation, at a starting salary of £1,002 per annum.

Applicants should have a good honours degree in Botany, Biology, Chemistry or Biochemistry and will be expected to register for a higher degree.

Further information may be obtained from Dr T. J. Flowers, School of Biological Sciences, University of Sussex, Brighton BN1 9QG. (268)

BRITISH SCHOOL OF ARCHAEOLOGY AT ATHENS

PHYSICAL CHEMIST

A postdoctoral **Research Fellow** will be appointed (for three years in the first instance) during the next few months to work in the School at Athens. He will be in charge of a small analytical laboratory using optical emission and X ray spectrometric techniques. There will also be some field work involving magnetometer surveys. Work at Athens would be preceded by a short period at the Research Laboratory for Archaeology, Oxford University. Salary range £2,300 to £3,000, depending on experience.

Applications in writing, giving details of education and experience, to Dr E. T. Hall, 6 Keble Road, Oxford. (306)

FANCY A CHANGE

We have vacancies galore at every grade in the scientific field, including marketing.

For further details, write or telephone:

WALBROOK APPOINTMENTS,
116 HIGH HOLBORN, LONDON, W.C.2.
Tel: 01-405 8787.

(3)

NATIONAL COUNCIL FOR SCIENTIFIC RESEARCH

Applications are invited from suitably qualified persons for the post of:

FOOD TECHNOLOGIST/ SCIENTIST

Applicants must have a postgraduate degree and experience in post-harvest physiology. Industrial or industry-related experience specializing in cold storage or freezing is desirable and some experience in microbiology would be an advantage. Candidates are expected to have background in fruit and vegetable processing with some training in food process engineering.

The successful applicant will conduct a research and development programme on the freezing storage of processed fruits and vegetables and the cold storage of fresh fruits and vegetables with emphasis on indigenous products. He will assist local food processors and other organizations in adapting this technology to local requirements and will also be required to train Professional and Technical Staff.

Salary according to qualifications and experience but a higher salary would be offered to exceptionally well-qualified and experienced senior scientists.

Professional Officers, K3,240 by K240 to K4,440; Senior Professional Officers, K4,680 by K240 to K5,640; Principal Professional Officers, K5,840 by K240 to K6,800.

For Zambians there is a superannuation scheme. Non-Zambians will be paid a gratuity of 25 per cent of aggregate basic salary earned during service of not less than thirty months.

Accommodation will be provided on an economic rental basis but not exceeding 10 per cent of basic salary. Hard furniture will be provided. For Non-Zambians travel and educational allowances are available for minor dependent children attending school outside Zambia.

Applications giving full personal details, qualifications, experience and naming three referees should be submitted to: The Secretary-General, National Council for Scientific Research, P.O. Box CH. 158, Chelston, Lusaka, Zambia. (359)

UNIVERSITY OF THE WITWATERSRAND

JOHANNESBURG

RESEARCH OFFICER IN CHEMISTRY

Applications are invited for the above-mentioned post in the Department of Chemistry to work on challenging synthetic and mechanistic aspects of novel organic and organometallic polymer systems. The applicant should hold a Ph.D. or equivalent degree in organic, physical-organic or organometallic chemistry and preferably should have one or two years' experience in demanding synthetic or physical-chemical experimentation. Only highly-motivated applicants with top academic records will be considered. The post, immediately available, will be contracted initially for two years at a salary of R5,500 (approx. £2,700) per annum, plus air fare.

The information sheet relating to this post may be obtained from the Registrar, University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, South Africa, or from the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications should be lodged not later than September 21, 1973. (300)

TECHNICIAN OR SENIOR TECHNICIAN

WESTERN INFIRMARY
Glasgow G11 6NT

DEPARTMENT OF PATHOLOGY

Applications are invited for the above post which has been provided in relation to the newly established immunopathology laboratory. The work includes a limited routine diagnostic service especially orientated towards renal and connective tissue diseases. Opportunities to participate in current research will be available. Further particulars of the duties involved may be obtained from Dr Keith Whaley, at the above Department. Salary according to Whitley Council conditions of Service.

Applications, with details of experience and qualifications together with the names and addresses of two referees, should be sent to the Hospital Secretary. (328)

UNIVERSITY OF DURHAM

DEPARTMENT OF CHEMISTRY

TEMPORARY EXPERIMENTAL OFFICER IN PHYSICAL-ORGANIC CHEMISTRY

Applications are invited for the post of Temporary Experimental Officer in the Department of Chemistry, to work with Dr D. L. H. Williams, on a kinetic study of certain aromatic rearrangement reactions using mainly spectrophotometric techniques.

Candidates should have a degree in Chemistry, or other equivalent qualification. It will not be possible to read for a higher degree.

The post will be for one year in the first instance with the possibility of an extension for a further period, on the salary scale: £1,641 × £75—£1,791 per annum with F.S.S.U.

Applications (3 copies) including a curriculum vitae and the names and addresses of two referees should be sent by September 3, 1973, to the Registrar and Secretary, Science Laboratories, South Road, Durham DH1 3LE, from whom further particulars may be obtained. (330)

UNIVERSITY COLLEGE, DUBLIN

DEPARTMENT OF PHYSIOLOGY

ASSISTANT LECTURER OR COLLEGE LECTURER

Appointment commences in October. Candidates should possess an M.B. or Ph.D. in Science (the latter in Physiology, Zoology or Pharmacology).

Salary scale:
Assistant Lecturer: £2,195 × 122—£3,049;
College Lecturer: £3,232 × 154—£3,386 × 148—£3,534 × 140—£4,234.

Family allowances are additional to salary. Non-contributory or F.S.S.U. type pension scheme available.

Applications (in triplicate) should indicate age, education, qualifications, prizes, experience and the names of three referees and be sent to the Secretary, Department of Physiology, University College, Merrion Street, Dublin 2, before August 27, 1973. (314)

UNIVERSITY OF LONDON

ST. BARTHOLOMEW'S HOSPITAL MEDICAL COLLEGE

DEPARTMENT OF BIOCHEMISTRY AND CHEMISTRY

RESEARCH ASSISTANT

Applications are invited from honours graduates in Biochemistry or related subjects to join a group studying the control of the citric acid cycle in mitochondria derived from nervous tissue. The appointment will be for 3 years and suitably qualified candidates may be able to register for a higher degree.

Applications, including a curriculum vitae and the names and addresses of 2 referees, to The Secretary, The Medical College of St. Bartholomew's Hospital, West Smithfield, London EC1A 7BE, quoting reference 589. (317)

COVENTRY HOSPITAL MANAGEMENT COMMITTEE

BIOCHEMIST (Basic or Probationary Grade) required for a post in the Group Laboratory with duties mainly at Coventry and Warwickshire Hospital. The successful candidate will have an honours degree in Chemistry or Biochemistry and will wish to pursue a career in medical biochemistry.

Opportunity will be available for further study for higher qualifications.

Salary and conditions of service will be in accordance with Whitley Council agreements.

Further particulars of the position may be obtained from Mr. R. W. Richardson, Group Biochemist, Coventry and Warwickshire Hospital.

Applications, with the names and addresses of two referees, should be sent to Coventry and Warwickshire Hospital, Stoney Stanton Road, Coventry before August 28, 1973. (318)

UNIVERSITY OF NEWCASTLE UPON TYNE

DEPARTMENT OF PLANT BIOLOGY

JUNIOR RESEARCH ASSOCIATE

Applications are invited for a Science Research Council Junior Research Associateship to work with Dr A. J. Richards on the cytogenetics of the *Hordeum murinum* aggregate. Candidates should have a good honours degree in Botany or Biology and should be prepared to undertake field-work in Turkey.

The appointment is tenable for three years commencing October 1, 1973, and the starting salary is at £1,236 per annum. (Salary scale under review.)

It is possible that suitably qualified applicants might be able to register for a higher degree.

Applications, together with a curriculum vitae, and the name of an academic referee, should be sent to: Dr A. J. Richards, Department of Plant Biology, Ridley Building, The University, Newcastle upon Tyne NE1 7RU before August 25, 1973. (350)

NATIONAL COUNCIL FOR SCIENTIFIC RESEARCH

Applications are invited from suitably qualified persons for the posts of:

BUILDING RESEARCH ENGINEER

BUILDING RESEARCH ARCHITECT

BUILDING MATERIALS SCIENTIST

Applicants for the post of Building Research Engineer must be engineers or technologists or architects with experience in construction research and development. Residential experience in tropical or sub-tropical areas of building would be desirable. The successful candidates will be required to develop a building research and development programme geared to the requirements of the Zambian construction authorities and industry.

Applicants to the post of Building Materials Scientist must be industrial chemists or engineers with wide experience in the production, usage and testing of building materials. The successful candidate will be required to establish a building materials laboratory service which will undertake research and development and give advice on the production and usage of building materials.

Salary according to qualifications and experience on the following salary scales:

Professional Officers, K3240 by K240 to K4,440; Senior Professional Officers, K4,680 by K240 to K5,640; Principal Professional Officers, K5,840 by K240 to K6,800.

Higher salaries may be offered to exceptionally highly qualified candidates with experience in relevant fields.

For Zambians there is a superannuation scheme. Non-Zambians will be paid a gratuity of 25 per cent of aggregate basic salary earned during service of not less than thirty months.

Accommodation will be provided on an economic rental basis but not exceeding 10 per cent of basic salary. Hard furniture will be provided. For Non-Zambians travel and educational allowances are available for minor dependent children attending school outside Zambia.

Applications giving full personal details, qualifications, experience and naming three referees should be submitted to: The Secretary-General, National Council for Scientific Research, P.O. Box CH. 158, Chelston, Lusaka, Zambia. (360)

WEST BIRMINGHAM HOSPITAL MANAGEMENT COMMITTEE

DUDLEY ROAD HOSPITAL

Applications are invited for the appointment of a PRINCIPAL GRADE BIOCHEMIST in the Department of Clinical Chemistry at Dudley Road Hospital. The Department is a busy and expanding one. The appointment will be mainly concerned with supervision and development of the automation section of the laboratory and the maintenance of quality control in that area. Whitley Council terms and conditions of service will apply (salary £3,516-£4,599). The Department may be visited by appointment with the Chief Biochemist Mr W. B. Yeoman (tel. 021-554 3801, ext. 330). Closing date for applications September 30, 1973. It is anticipated that interviews will be held mid-October.

Applications to Group Personnel Officer, Dudley Road Hospital, P.O. Box No. 293, Dudley Road, Birmingham B18 7QH. Ref. 125. (345)

UNIVERSITY OF LONDON KING'S COLLEGE

DEPARTMENT OF PHARMACOLOGY

Applications are invited for a POST-DOCTORAL RESEARCH ASSISTANTSHIP in Biochemical Pharmacology. The position is for one year initially, with provision for extensions for up to two further years, salary in the range £1,599 × 165 per annum plus £162 London Allowance. Supporting technical assistance is available. Applicants preferred with interests and experience in transmitter synthesis and turnover in brain, in the isolation and characterization of isoenzymes, or in immunohistofluorescence procedures.

Write to Dr A. K. Prince (N), Department of Pharmacology, King's College London, Strand, London WC2R 2LS as soon as possible. (335)

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE

UNIVERSITY OF LONDON

DEPARTMENT OF BIOCHEMISTRY

Applications are invited for the post of RESEARCH TECHNICIAN, supported by an MRC grant, for work on the biochemistry and biology of cell and membrane fusion. The post is available for one year in the first instance, with possibility of renewal until July 31, 1976.

Applications with curriculum vitae and names of two referees should be sent as soon as possible to Professor J. A. Lucy, Department of Biochemistry, Royal Free Hospital School of Medicine, 8 Hunter Street, London WC1N 1BP. (260)

BIOCHEMIST REQUIRED

to work on problems concerning the separation of peptides from plasma urine and brain tissue. The post will be Basic or Senior grade according to qualifications and experience. Applications, together with the names and addresses of two referees, to Professor H. E. de Wardener, Department of Medicine, Charing Cross Hospital Medical School, Fulham Hospital, London W6 8RF. (305)

JAMES COOK UNIVERSITY OF NORTH QUEENSLAND

SENIOR TUTOR IN MARINE BIOLOGY

Applicants should have a higher degree in zoology, marine biology, or biological oceanography. Previous teaching experience at undergraduate level is desirable. Duties will include active promotion of and participation in research programmes and graduate training, the organization of some undergraduate specialist courses in marine biology, and the organization of field work on the University's research vessel.

Salary range: $A7,270-$A8,698 per annum, plus locality allowance of $A142 per annum for a married male or $A71 per annum for a single appointee. Conditions of appointment include F.S.S.U. superannuation, invalid pension scheme, housing assistance, study leave and allowance for travel and removal expenses on appointment.

Additional information and application forms may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications close on September 14, 1973. (302)

NATIONAL COUNCIL FOR SCIENTIFIC RESEARCH

Applications are invited for the post of:

TEXTILE TECHNOLOGIST

Candidates must have a degree or diploma in textile technology and more than three years' experience in the textile industry. The successful candidate will be required to carry out cotton and other fibre testing as well as yarn and fabric testing. He will also be expected to carry out determination and evaluation of other fibre properties. Knowledge of cotton fibre and general textile processing and production will be an added advantage.

Salary according to qualifications and experience on the following salary scales: Technical Officer Grade I: K2,900 by K180 to K3,440 by K240 to K4,640; Professional Officers: K3,240 by K240 to K4,440; Senior Professional Officers: K4,680 by K240 to K5,640.

For Zambians there is a superannuation scheme. Non-Zambians will be paid a gratuity of 25 per cent of aggregate basic salary earned during service of not less than thirty months.

Accommodation will be provided on an economic rental basis but not exceeding 10 per cent of basic salary. Hard furniture will be provided. For Non-Zambians travel and educational allowances are available for minor dependent children attending school outside Zambia.

Applications giving full personal details, qualifications, experience and naming three referees should be submitted to: The Secretary-General, National Council for Scientific Research, P.O. Box CH. 158, Chelston, Lusaka, Zambia. (361)

INSTITUTE OF ·UROLOGY

(University of London)

in association with St. Peter's Hospitals

Applications are invited for a RESEARCH FELLOW (with medical and/or scientific qualifications), in the grade of Lecturer (Senior Registrar status), for an investigation into the ultrastructure of the kidney and urinary tract epithelium. The successful applicant will be attached to the Electronmicroscopy Unit in the Department of Pathology, St. Paul's Hospital. Appointment for one year in the first instance, subject to renewal.

Applications to the Pathologist, St. Paul's Hospital, Endell Street, London W.C.2. (342)

UNIVERSITY OF ABERDEEN

POSTDOCTORAL RESEARCH FELLOW IN ORGANIC CHEMISTRY

Applications are invited for the above post for synthetic work in the steroid field. The successful applicant will be required to contribute to the undergraduate teaching programme of the Department. The appointment is for two years. Salary within range £1,929 to £2,223 with initial placing according to age and experience.

Further particulars from The Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by September 8, 1973. (357)

SENIOR TECHNICIAN (Grade 5, salary: £1,881 to £2,241) wanted October for small university laboratory, to assist with biochemical and biological work, and in addition, general duties in laboratory. Pay and conditions on university restructured scale.—Apply Administrator, Nuffield Laboratory of Ophthalmology, Walton Street, Oxford. (297)

UNIVERSITY OF WARWICK

RESEARCH TECHNICIAN GRADE 3

The Department of Biological Sciences has a vacancy for a permanent post in the Research Laboratories. The person appointed will work under the direct supervision of academic staff on the biochemistry of proteins and nucleic acids. Salary in the range £1,539×51—£1,794 per annum.

Applications in writing to the Academic Registrar, University of Warwick, Coventry CV4 7AL, quoting ref. 2/T/73, as soon as possible. (343)

TECHNICIAN

required immediately for cytogenetics laboratory concerned with pre- and post-natal diagnosis of birth defects and of inter-sex states. Some experience of chromosome work or tissue-typing would be an advantage. Salary according to Whitley Scale.

Applications, with details of experience and the names of two referees, to Dr R. Robert Harris, Department of Medical Genetics, St. Mary's Hospital, Hathersage Road, Manchester M13 0JH. (341)

UNIVERSITY OF READING

RESEARCH DEMONSTRATOR required in Department of Physiology and Biochemistry. The successful applicant will act as a demonstrator in the department and will carry out research for a higher degree on the structure and function of RNA polymerase. Salary £1,047×51—£1,149 p.a.

Apply by August 31 to Senior Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH, quoting reference TN54. (316)

RESEARCH DEMONSTRATOR

in Physical Geography required in Department of Geography, University of Reading, for three years from October 1, 1973, to assist in photo interpretation in Physical Geography during practical courses. Salary scale £1,047 by £51 to £1,149 per annum.—Applications with full details of training and experience and the names of two referees should be sent to arrive not later than August 31, 1973, to Professor R. A. G. Savigear, Department of Geography, University of Reading, Whiteknights, Reading RG6 2AF, ref.: TN45. (356)

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UNIVERSITY OF HULL

DEPARTMENT OF PLANT BIOLOGY

Applications are invited for a post as

TECHNICIAN (GRADE 3)

to assist the Professor of Genetics. The work will involve mainly research but some preparation of teaching material will be required. Research is concerned with chemical and other interactions between species, particularly in relation to cyanogenesis by plants. Although preference will be given to those candidates with experience of enzyme work, applications from those with a wide knowledge of laboratory practice in Biology will be welcome. Minimum qualifications: O.N.C. or equivalent with 3-5 years' relevant experience. Salary on scale £1,539 to £1,794.

Applications including the names of two referees to the Technical Staff Officer, the University, Hull, quoting Ref. TPB/1, by September 1, 1973. (261)

UNIVERSITY OF READING

RESEARCH ASSISTANT required in Department of Microbiology to work on the ecology and serology of Pathogenic and non-pathogenic *Erwinia* spp. Applicants should have a first or second class honours degree in Microbiology or related subjects. Salary £1,475 per annum approximately or equivalent of ARC studentship if a candidate is accepted for a higher degree.

Apply with full details, quoting reference MN54, and stating the names of two referees before August 31, 1973, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH. (337)

FELLOWSHIPS AND STUDENTSHIPS

UNIVERSITY OF KENT AT CANTERBURY

RESEARCH FELLOWSHIP IN THE BIOLOGICAL LABORATORY

Applications are invited from suitably qualified candidates in microbiology, bacterial genetics or molecular biology for a post-doctoral fellowship involving a study of colicin factors. Salary (from October 1, 1973) in the range £1,929 to £2,223.

Application forms and particulars may be obtained from the Assistant Registrar, Faculty of Natural Sciences, Chemical Laboratory, The University, Canterbury CT2 7NH, Kent, to whom completed applications should be submitted by August 24. Please quote Ref. A.33/73. (280)

MEMORIAL UNIVERSITY OF NEWFOUNDLAND

Canada

DEPARTMENT OF BIOCHEMISTRY

Applications are invited for a POSTDOCTORAL FELLOWSHIP to work on the mechanisms of oxidation of xenobiotics in marine crustaceans. The post is tenable for one year in the first instance and may be renewed for a further year. The salary will be $8,600 per annum.

Applications, accompanied by a curriculum vitae and the names of two referees, should be sent to Dr E. A. Barnsley, Department of Biochemistry, Memorial University of Newfoundland, St. John's, Newfoundland, Canada. (301)

UNIVERSITY OF LIVERPOOL

DEPARTMENT OF ORGANIC CHEMISTRY

Applications are invited for a C.A.P.S. STUDENTSHIP (supervisors Dr R. J. Abraham and Dr W. A. Thomas) for an investigation on the conformation of biologically active molecules in solution by theoretical calculations and multinuclear N.M.R. Spectroscopy.

Candidates should hold an upper second class honours degree and an interest in computation and/or N.M.R. would be required.

Applications should be sent to The Registrar, The University, P.O. Box 147, Liverpool L69 3BX. Quote Ref. RV/N/80419. (256)

UNIVERSITY OF ABERDEEN

RESEARCH FELLOWSHIP IN ZOOLOGY

Applications are invited for above post supported by the Science Research Council on a project involving comparative neurophysiology in collaboration with Dr D. M. Guthrie. Applicants should preferably have experience of electro-physiological methods applied to invertebrate material. Appointment is for two years from October 1, 1973. Salary in range £1,929-£2,058.

Further particulars from The Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged as soon as posible. (309)

CSIRO

AUSTRALIA

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas. The organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

RESEARCH FELLOW

DIVISION OF FOOD RESEARCH

LOCATION: **MEAT RESEARCH LABORATORY**
BRISBANE, QLD.

The fellowship is offered for research into one of the following subjects, all of which are of major importance to the laboratory's research programmes:—

1. Qualitative and quantitative changes in myofibrillar proteins during onset of rigor mortis, and during post-rigor treatment of muscle prior to cooking.
2. The role of proteoglycan in connective tissue structure and function.
3. Factors affecting the survival of bacteria on meat surfaces subjected to drying, chilling and freezing.
4. Physico-chemical interactions between muscle proteins and proteins derived from plant sources.
5. Isolation and identification of the flavour principles of sheep meats.

The laboratory has a total staff of 90, of which over 30 are professionally qualified. It is well equipped for the performance of chemical, biochemical, physiological, microbiological and electron miscroscope work and is supported by adequate computer and workshop facilities.

QUALIFICATIONS: A Ph.D. degree in the appropriate discipline or equivalent qualifications, and demonstrable research ability. Research experience *must* include recent studies in one of the areas outlined above.

CONDITIONS: The appointee will be offered a salary within the range of $A8,489–$A12,932 p.a. although an outstanding applicant could be offered up to $A15,454 p.a. Appointment will be for three years without option of renewal and return fares will be paid for the Fellow and his family upon satisfactory completion of the term of appointment.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting reference number 300/607, should reach:—

The Personnel Officer,
Australian Scientific Liaison Officer,
64–78, Kingsway, LONDON, WC2B 6BD

by the 14th September, 1973.

Applications in U.S.A. and Canada should be sent to:
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(304)

UNIVERSITY OF BRISTOL

LONG ASHTON RESEARCH STATION

ERNEST COOK POSTGRADUATE STUDENTSHIP

Applications are invited from holders of good honours degrees or equivalent qualifications (e.g., Grad.R.I.C. or M.I.Biol.) in Chemistry, Biology or Biochemistry, for a studentship offered by the Ernest Cook Trust of Fairford at a value of £700 per annum for three years to study the antifungal activities of chemicals which might be effective in controlling Dutch Elm disease. The work is a collaborative project between Dr D. Woodcock and Mr D. R. Clifford of Long Ashton Research Station and Dr J. N. Gibbs of the Forestry Commission, Alice Holt Lodge, Surrey. The successful applicant may register for a higher degree of the University of Bristol.

Application forms from the Secretary, Research Station, Long Ashton, Bristol BS18 9AF, should be returned by September 15, 1973. (285)

UNIVERSITY OF WARWICK

POST-DOCTORAL FELLOWSHIP IN BIOLOGICAL SCIENCES

Applications are invited for the above post to work on the use of cell fusion techniques to study the multiplication of RNA animal viruses especially influenza. The post would be suitable for a virologist with a good knowledge of biochemistry or for a biochemist or cell biologist with an interest in animal virology. The appointment is for one year, commencing November 1, 1973. Salary in the range £1,929× 129—£2,058 per annum with F.S.S.U.

Further details and application forms may be obtained from the Academic Registrar, University of Warwick, Coventry CV4 7AL, quoting ref. 2/Q/73. Closing date for receipt of applications is September 10, 1973. (344)

THE OPEN UNIVERSITY

RESEARCH STUDENTSHIP IN CHEMISTRY

Applications are invited for a full-time Research Studentship tenable from October 1 or as soon as possible thereafter. The candidate is expected to work on the theoretical interpretation of N.M.R. shifts of nuclei other than hydrogen (^{13}C, ^{14}N, etc.) under the joint supervision of Dr Joan Mason (Open University, Walton Hall) and Dr Ruth M. Lynden-Bell (Cambridge). The student will be expected to register for a higher degree of the Open University.

Applicants should possess an honours degree (first or second class) in chemistry. The value of the studentship is £695 per annum, plus the usual allowances.

Further particulars and application forms are obtainable from The Higher Degrees Office, The Open University (Cl), P.O. Box 49, Walton Hall, Milton Keynes MK7 6AA.

Closing date: September 1. (266)

UNIVERSITY OF KENT AT CANTERBURY

CASE STUDENTSHIP IN BIOCHEMISTRY

Applications are invited from candidates holding a first or upper second class honours degree in biochemistry or a related subject for a CASE research studentship to participate in a comparative study of animal host and protozoal parasite enzymes in collaboration with the Wellcome Research Laboratories, Beckenham, Kent. No prior knowledge of protozoology is required.

Application forms and details may be obtained from the Assistant Registrar, Faculty of Natural Sciences, Chemical Laboratory, The University, Canterbury CT2 7NH, Kent. Please quote ref. PG14/73. Closing date for applications August 31. (327)

UNIVERSITY OF STRATHCLYDE
DEPARTMENT OF PURE AND APPLIED CHEMISTRY

Postgraduate Studentship

Applications are invited from suitably qualified chemists or biochemists for an SRC/CASE Postgraduate Studentship in collaboration with Pfizers Limited.

The project, which will commence in October 1973, involves exploration of the scope of a novel synthesis of certain heterocyclic compounds and assessment of their usefulness in biological systems.

Applications to Dr. G. R. Proctor, Department of Pure and Applied Chemistry, Thomas Graham Building, University of Strathclyde, 295 Cathedral Street, Glasgow G1 1XL as soon as possible giving full curricular details.

(255)

LECTURES AND COURSES

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The Polytechnic of Central London

Medical Applications of Acoustics

A series of ten one-hour lectures Thursdays 6.00–7.00 pm starting 4 October 1973. A continuation of the PCL's tradition of lectures in physics applied to medicine, the course includes contributions from PCL staff, as well as Dr A. Fourcin (University College London), Dr J. D. Hood (National Hospital for Nervous Diseases), Dr J. J. Knight and Mr N. Shah (Institute of Laryngology and Otology) and Mr M. C. Martin (Royal National Institute for the Deaf).

No specialist knowledge will be assumed and no minimum qualifications called for, but those interested will be expected to have at least a pass degree/2nd MB. Fee: £4; further details from Dr J. A. Simmons, Department of Physics, The Polytechnic of Central London, 115 New Cavendish Street, London W1M 8JS. Tel 01-486 5811.

(338)

UNIVERSITY OF LONDON
KING'S COLLEGE
DEPARTMENT OF CHEMISTRY
RESEARCH STUDENTSHIP

Applications are invited for a RESEARCH STUDENTSHIP, available from October 1, 1973, for studies in organophosphorus chemistry. The value of the award will be equivalent to an S.R.C. Studentship and the successful candidate will be able to register for a Ph.D. degree.

Applications, giving a full curriculum vitae and the names of two referees, should be sent as soon as possible to Dr C. D. Hall (N), Department of Chemistry, King's College, Strand, London WC2R 2LS. (312)

APPOINTMENTS WANTED

NUMERICAL ANALYST

seeks challenging position. Ph.D. (1968, University of Wisconsin) in computer science. 12 years computer programming experience, 3½ years industrial research experience. Research interests, publications in approximation theory, sparse matrices, stiff differential equations. Will consider academic, governmental or industrial research position. Available immediately. Speaks English, Dutch, some French, a little German. No geographic restrictions. Enquiries to Box No. 310, Nature, T. G. Scott & Son Ltd., 1 Clement's Inn, London WC2A 2ED. (310)

GRANTS & SCHOLARSHIPS

UNIVERSITY OF MANCHESTER
INSTITUTE OF SCIENCE AND TECHNOLOGY
DEPARTMENT OF CHEMISTRY

Applications are invited from British graduates, Grad. R.I.C., etc., for grants for Ph.D. research in:

(1) Diels-Alder Reactions of Allenes.
(2) Platinum Co-ordination of Complexes and their Biological Activity and Use.

Applicants should write as soon as possible to Professor R. N. Haszeldine, Department of Chemistry, U.M.I.S.T., P.O. Box 88, Manchester M60 1QD.

(319)

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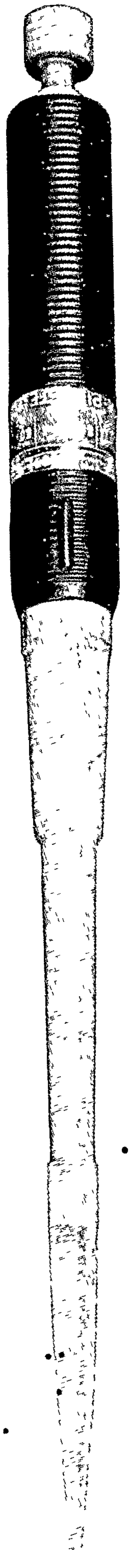

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AUGUST 24 1973

Nature in the Future

It ill becomes a journal to waste too much of its space on introspection, as John Maddox stressed in his last editorial (May 18 of this year). In the long run, *Nature* will prosper or not on the strength of its actual, not its avowed, editorial policy. Nevertheless, a new Editor may be excused a little public musing on what he sees for *Nature* if only because of the intimacy that exists between the journal and its readership and to which Mr Maddox alluded. Many of *Nature*'s regular readers would expect a new Editor to explain himself though none should require him to show all his cards nor to deliver all his promises in the too-immediate future.

It is the quality of the papers submitted to *Nature* which ultimately controls its success or failure. Good as one hopes the journal will be from beginning to end, it is clear that a stream of second-rate scientific papers would be the quickest road to oblivion. Thus an Editor's first responsibility is to ensure that the standard of papers is high. This is, of course, a task which it would be impossible to perform without a diligent staff and a small army of patient reviewers, but at the centre of it lies the editorial question—"Is it a *Nature* paper?" No two people would agree on the definition of a *Nature* paper, but some common ground is clear. Many a thoroughly correct and readable manuscript has to be declined for lack of something which sets it apart as helping to see the world through a newer and better window. On the other hand room has to be found for the speculative paper in which cast-iron evidence cannot be adduced but which has the potential to open up new fields of research.

Two specific points should be made concerning scientific papers. The first is one of growing concern to all connected with the production of the journal—brevity. In *Nature*'s centenary number (November 1, 1969) a few of the journal's most exciting papers were reprinted. It was something of a surprise to find that in the 1930's the Cockcroft–Walton generator could be announced in less than 300 words and the fission of uranium postulated in less than a page. Brevity was not confined to the physicist. In 1953, the structure of DNA was announced in one page. With some justification one can argue that science is now bigger, techniques are more complex, and so on. Yet *Nature* simply cannot in the foreseeable future expand to accommodate longer papers, nor is it all clear that readers would wish us to do so. Scientists-as-readers seem to demand more brevity than scientists-as-writers are prepared to give.

The second point is a personal dislike for papers in which all bets are hedged. A J Leibling, a highly perceptive observer of the press, used to write of the "ademonai-kodemonai" (Japanese for "on-the-one-hand-this-on-the-other-hand-that") syndrome amongst journalists with lots of possibilities to juggle stemming from one hard but at present uninterpretable fact. Americans will recognize this syndrome amongst their political commentators. We would rather carry the simple observation unadorned than have it smothered in unhelpful ademonai-kodemonai.

Reassurance ought to be given to those who view the change to one *Nature* per week in January 1974, announced recently, as reflecting some radical switch in editorial policy. This is not so. Many ingredients of course have gone into the making of this decision and the editorial view is only one of them. But it has been clear after many conversations with contributors and readers that there was a preference for a unified weekly. The amount of space for contributions will remain roughly the same as that which is now available in the three journals.

Scientific papers are our bread and butter, but it will be obvious that the amount and quality of the jam has also improved over the past few years in coverage and exposition of science and its news and politics. The aim will be to increase the scope of these sections and to prevent their developing into bland reporting. Fine words, but what do they mean in practice? *Nature*'s news gathering facilities around the world must grow in the next year or two, as it is increasingly necessary to understand the scientific scene away from the trans-Atlantic axis. Furthermore, *Nature* must be an open journal, reflecting the sense of community which is still very strong amongst scientists. In the long run much of *Nature* is simply scientists talking to scientists about things which have a broad interest. Opinions differ about what constitutes "broad interest" and we can make no claim that the exposition and opinion sections of the journal give a uniform and totally balanced coverage. But the remedy to that is in the hands of readers. If you think there is more to tell or another side to a story, let us hear it.

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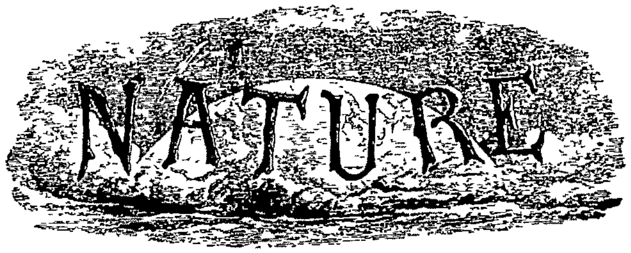
100 Years Ago



> A day will come when every great Administration will have its Consulting Committee, composed almost exclusively of men of science, and then many mistakes will be avoided, and many forces utilised which are at present lost. But in order that such an institution should be born and developed, it is necessary that the function of Science be universally comprehended and accepted. To attain this result is one of the chief aims of the French Association.

From *Nature* 8, 349, August 24, 1873

OLD WORLD

Dr Zhores Medvedev Replies to Professor John Ziman

DEAR PROFESSOR ZIMAN,

I have read your "Second Letter to an Imaginary Soviet Scientist" with great interest (*Nature*, **243**, 489, 1973) I doubt whether you have received many replies from the USSR As you probably remember, your first letter (*Nature*, **217**, 123, 1968) did not induce many replies either My own reply sent to you in April 1968 started our correspondence and friendship, and I explained to you then that in the photocopied version of *Nature* which was available in the USSR your letter was not reproduced at all so that only a few scientists in the USSR have known of your appeal I can add now that even though the USSR has signed the Universal Copyright Convention, which does not permit the distribution of photocopies of *Nature*, your second letter has also only been seen by few people in the USSR because this page was simply cut out from the copies of *Nature* in Soviet libraries

As you know I was officially invited to Britain in January, but a few weeks ago the Soviet authorities unexpectedly deprived me of my citizenship, a decision made partly on the basis that according to them the invitation was private But I assure you that I had thought of answering your letter before this unhappy development—at a time when I was legally one of those to whom you addressed your letter

In your second letter you asked us to say whether the boycott of conferences and symposia in the USSR would help those Soviet scientists whose human rights are being violated You are right to say that there is no simple answer and that, in general, the boycott of scientific meetings is not a good way to help those who are in trouble I am sure that the isolation of the Soviet scientific community does not help Soviet scientists During recent years, in spite of many troubles at home, I was usually very glad to meet foreign colleagues in the USSR These meetings gave me great moral support and they had a significant influence on my research work But when you arrive in the USSR there are several approaches you can take You can, for example, ignore the official ceremony and have private meetings with friends or colleagues whom you like and want to support But, of course, if you find that such friendly contacts with individuals are impossible because of interference from bureaucrats or the police, then you certainly have to make a protest or return home But the situation which faces foreign scientists could be more complex than that I give you one such example

The World Psychiatric Association will hold an international symposium on "Aspects of Schizophrenia" in the USSR next October The Soviet hosts have selected two very attractive Caucasus cities Two days of meetings will take place in Yerevan and two others in Tbilisi The ministers of health of both republics, Armenia and Georgia, will give opening addresses Armenians and Georgians are very nice and traditionally open and hospitable people I am sure that British, French and other foreign participants at this symposium will have a very good time

But there are other problems which cannot be ignored Among the speakers are A V Snezhnevsky, G Morosov and R A Nadzharov who were responsible for many decisions which sent some political "dissidents" into psychiatric prison–hospitals Two scientists, Dr Leonid Plyshch and Yury Shikhanovitch, have been their most recent victims You probably remember that the same three psychiatrists examined me in 1970 and the methods of their "work" have been described in the book *Question of Madness* written by my brother and I There have been several other protests about abuses of psychiatry in the USSR and the forthcoming symposium with these three "heroes" of many well-known psychiatric–political cases present is a unique chance for western scientists to investigate these accusations at first hand

I do not suggest that western scientists try and obtain first hand knowledge of some political "patients", for they will not be allowed to do so I am sure that A Snezhnevsky and G Morosov will always be able to produce for foreign observation some clear mental syndromes even in local Caucasus clinics But there is a more general aspect of the problem which honest scientists cannot ignore

On August 8, 1973, Professor R Nadzharov distributed through Tass a statement which said that suggestions about the use of psychiatry to punish "different-minded people are a part of an anti-Soviet propaganda campaign launched by hired professional anti-Sovietists" Professor Nadzharov explained that " the Soviet laws in this field are in principle similar to the laws operating in most other countries and that the Soviet laws specifically provide legal punishment for the persons guilty of unjustified placing of the patient in a mental hospital" Nadzharov noted that all slanders about abuses of psychiatry in the USSR had been rejected by the World Association of Psychiatry That the world association has in the past

Conference On Aspects of Schizophrenia

ACCORDING to the preliminary announcement of the International Conference on Aspects of Schizophrenia to be held in Yerevan and Tbilisi in the Soviet Union from October 8 to October 12, 1973 the following are to be present

H P Rome (USA), A V Snezhnevsky (USSR), S Follin (France), A Megrabyan (USSR), H Rennert (East Germany), G Morosov (USSR), J J López Ibor (Spain), R A Nadzharov (USSR), L Eisenberg (USA), C Koupernik (France), M Vrono (USSR), V Bashina (USSR), R de la Fuente (Mexico), E Stromgren (Denmark), J K Wing (Britain) H Collomb (Senegal), Z Serebryakova (USSR), G Hunter (FRG), Z Zharikov (USSR), K Heinrich (West Germany), R F Prien (USA), M H Lader (Britain), P C Baastrup (Denmark), A Smulevitch (USSR), R Gardner (Britain), Yu Saarma (USSR), W Linford Rees (Britain), A Zurabashvili (USSR), A J Coppen (Britain), I Yamashita (Japan), A J Mandell (USA), J M Davis (USA), A Freedman (USA), C E Frohman (USA), R Lideman (USSR), D Lozovsky (USSR), B Grbeša (Yugoslavia), S Semyonov (USSR), G Kolyaskina (USSR), K Seidel (East Germany), T Asuni (Nigeria), L Erlenmeyer-Kimling (USA), E Inouye (Japan), V Gindilis (USSR), J Nielsen (Denmark), A Falek (USA), D Leigh (Britain), J Angst (Switzerland), G Winokur (USA), I Shakhmatova (USSR), T Imura (Japan), F Kontridze (USSR), M Mestiashvili (USSR) and S Zulidze (USSR)

ignored all appeals about the abuse of psychiatry is probably true, but I can hardly agree with other statements by Nadzharov. I do not want foreign psychiatrists to boycott this meeting. But I hope very much that between official meetings and dinners, receptions and parties, excursions and ceremonies, some Western scientists will ask their Soviet colleagues a few specific questions. These might be some of them:

(1) Which articles of the acting legal codes in the USSR make psychiatrists punishable for unjustified placing of patients in a mental hospital?

(My reply: There is no such article in the acting legal code, because it was eliminated in 1961. In the acting legal code there is an article No. 126 which makes "illegal deprivation of freedom" punishable. An addendum to this article indicates that illegal deprivation of freedom can be considered as a crime only when a private person made this deprivation. In another article of the code (No. 178) which considers the illegal deprivation of freedom or arrest made by officials, psychiatrists are not mentioned at all.)

(2) Did the defence lawyers have the opportunity to nominate psychiatrists to observe and diagnose in any known political case?

(My reply: No. In practice the psychiatric team for political cases is selected by the prosecution and the administrators of psychiatric institutions. In most cases the nomination of such teams is the responsibility of G. Morosov, Director of Serbsy Institute of Forensic Psychiatry. Psychiatrists recommended by lawyers or relatives have never been incorporated into such teams.)

(3) Why is it that for non-political crimes the psychiatric clinics local to the courts decide on the mental health of the accused but in most political cases the decisions about mental health are always given by the same team of Moscow psychiatrists? Why was A. Snezhnevsky from Moscow the psychiatrist who advised on the case of Leonid Plyshch in Kiev?

(My reply. Because most accused persons are investigated for something they wrote or published in "samizdat". The prosecution cannot allow any local psychiatrist to read such publications and therefore only a few specially trusted and high ranking psychiatrists "trained" to study manuscripts can solve the problems of dissidents.)

(4) Why are political dissidents like Leonid Plyshch sent, after psychiatrical investigation, not to the general psychiatric clinics, like most common insane criminals, but to the prison-like hospitals which according to Article 59 of the Legal Code can be used only for persons who have committed "crimes of specially grave danger" and where they are usually deprived of any rights and possibility of communications with relatives and lawyers? And why are they kept there longer than allowed by the articles of the code under which they had been tried?

(My reply: I cannot explain this cruelty for people whose only "crime" is writing or distributing some kind of information.)

I would like foreign participants of this symposium to compare my replies with those they will receive from their Soviet colleagues. I would also like the British experts who will be attending this symposium to invite this special team of Soviet experts of political psychiatry to London. They could bring them to Hyde Park during the weekend to observe people speaking at spontaneous meetings. Then it will be possible to see whether the attitude of the psychiatrists to dissidents is really the same in Britain as it is in the USSR. It will be interesting to know whether Professor G. Morosov, Director of the Serbsky Institute of Forensic Psychiatry, and Professor A. Snezhnevsky, Director of the Institute of General Psychiatry, see any of the speakers and the audience as possible patients if Hyde Park were not in London, but in Moscow.

I do not advise British colleagues, however, to ask this team about my own mental state. They probably have already forgotten about my case. Recently a medical friend of mine in Britain described my own situation quite clearly. "You came to Britain after you published a book which criticized the restrictions of travel for Soviet scientists. You published in Britain a new book about Solzhenitsyn. The Supreme Soviet Praesidium deprived you of your citizenship and the Soviet Embassy here confiscated your passport. And you still hope and want to return to the USSR and you also think this will be possible? You are really mad!"

Yours sincerely,

ZHORES A. MEDVEDEV

National Institute for
Medical Research,
Mill Hill, London

BRITISH ASSOCIATION

Sir Kingsley's Appeal

THE British Association for the Advancement of Science returned to the cathedrals this week. After the relative informality of last year's Leicester meeting, this year's got under way with a grand procession into Canterbury Cathedral for the conferring of degrees, the singing of a token hymn (appropriately enough "Who would true valour see, let him come hither"), and the hearing of the Presidential Address.

The last part of the operation was most worthwhile. Sir Kingsley Dunham's speech was a stern warning by a moderate man that more attention must be paid to environmental science. "The question," Sir Kingsley said, "is quite simply, can our species survive for the next few hundred years? This dilemma is being presented at a moment when for the first time ever the techniques of systems analysis make it possible to begin to attempt to handle the considerable number of variables in the environmental picture even though verification is admittedly difficult".

"When a full assessment, based on adequate input becomes possible, it may show that economic growth has to be limited or that a more equitable distribution of its benefits must be made".

Sir Kingsley Dunham

Discussing *The Limits to Growth* and the work of Professor Forrester's group at MIT, Sir Kingsley said that it gives "in a concise form, an alarming picture which if it is correct calls for very prompt action". Sir Kingsley's criticism of the work is that the input data are inadequate. "My plea," he said, "is for the advancement of environmental science to the point where we have convincing data to work with, a reliable input for penetrative systems analysis such as could be attempted by the International Institute of Applied Systems Analysis near Vienna."

"Great moral issues almost certainly lie ahead and if it falls to environmental scientists to point the way to them, we cannot shirk the issues and say that they are none of our business . . . for more than one thousand years, the predicament of man has been thought about, talked about and prayed about in this place, the mother church of English Christendom. Like those who came before us, I believe that most of us accept the paramount values embodied in the Pauline virtues of faith, hope and charity; of which the greatest is charity in its broadest sense. But we cannot but recall that neither the Christian religion nor Science offers the expectation that man will flourish in perpetuity upon the Earth. To early Christians the apocalypse seemed close. To those of us having some acquaintance with palaeontology, the fact that a greater number of species have become extinct than have survived is warning enough, some of these, like the ammonites, having vanished abruptly from the record after a great population explosion. Prudence demands that no effort be spared to advance those sciences which should be able to show whether the threat is real or imagined, close or distant."

"The position in the physical environmental sciences," Sir Kingsley said, "is that there is a pressing need for more widespread and exact surveys. These include surveys of mineral and hydrocarbon wealth, work on alternative energy sources such as solar energy and an assessment by meteorologists and oceanographers of the risk of the temperature of the atmosphere and seas being raised to an extent dangerous to life by increased waste heat from the energy used to produce a high standard of living throughout the world."

Sampling and surveys are equally important in the life sciences, Sir Kingsley said. So far most biologists can give only a hindsight interpretation of changes, not a prediction. Yet prediction is of the utmost importance within the framework of human ecology.

The widely separated positions held about the dangers of pollution, Sir Kingsley said, is "a measure of the inadequacy of the data so far at the disposal of scientists and economists."

A large scale chemical monitoring programme is needed, and a governmental programme of monitoring for substances other than radio isotopes is likely to be set up in the wake of last year's Stockholm conference.

"The data collecting here advocated is of the nature of survey work, but I see as the urgent task of environmental science to secure the complex information needed to test old hypotheses and to establish new ones."

Turning to the financing of this work Sir Kingsley questioned whether the resources available at present are sufficient. "I am myself too deeply involved to attempt to answer that question: it must suffice to say that . . . the cost of the effort does not amount to much more than one 0.1% of our national income."

With Sir Kingsley's speech as a keynote the conference is under way with a number of contributions running along similar lines.

A symposium on reserves, utilization and recycling of mineral wealth is part of the programme, and Sir George Porter, Director of the Royal Institution, opened the Chemistry Section meetings by declaring that "the lights will not go out in the 21st century" because chemical systems for utilizing and storing solar energy will be developed.

Fifteen hundred people had materialized in Canterbury, at the University of Kent, by the start of the meeting, which is the first to be ruled by the association's slimmed-down committee structure. The first elected members of the general committee and council will be voted in during the course of the meeting.

FUSION

Design Team at Culham

A EUROPEAN team is to start work this month on the design of a large fusion experiment at the UK Atomic Energy Authority's Culham Laboratory. The study—which is to be carried out under the auspices of Euratom—is to be led by Dr Paul Rebut, a French engineering physicist. A team of about 20 physicists and engineers will be involved in the design of a tokamak system which is intended "to provide plasma conditions more advanced than would be obtainable in the American and Russian devices presently under construction", according to Dr R. S. Pease, Director of Culham.

The design work will take between eighteen months and two years, after which it is hoped to move immediately into construction of the experiment. The design study now proposed means that British plans announced last May to build a similar large experiment have been merged into the Euratom effort (*Nature*, **243**, 51 ; 1973). At present, and probably for the first six months of the study, the work is being carried out under existing contracts of association with Euratom, but further funds and detailed approval from Euratom will be needed after that period. The design team is due to report on its progress to a European committee on fusion after six months.

EEC

Chairman for CERD ?

LORD KENNET, the opposition spokesman on Foreign Affairs and Science Policy and one of the three British representatives on CERD, has been appointed as an adviser to the European Commission for one year. Lord Kennet succeeds Professors Aigrain of France and Casimir of the Netherlands.

Lord Kennet's appointment is very much a part-time job—a spokesman for the commission said last week that it involves about two days work a month. As adviser it is likely that Lord Kennet will take over as chairman of CERD, the advisory body which was set up last April to aid the commission on research and development matters.

But Lord Kennet's appointment does not mean that a full-time adviser to the commission will not be appointed. The intention is still, according to a spokesman, to appoint a scientific adviser to the President of the Commission, but as yet there are no signs that such an appointment is imminent.

At a recent meeting it was suggested that CERD should be divided into subgroups to concentrate on different aspects of research and development. This recommendation will be discussed again at the next meeting of CERD on September 17. If the fission of CERD goes ahead, then Lord Kennet will probably be responsible for the coordination of the work of the different groups.

OPEN UNIVERSITY

Links and Links

AN enthusiastic student at the Open University is attempting to forge links between the university and both the Royal Institution and the British Association for the Advancement of Science. In the August issue of *Sesame*, the university's newspaper, Mr Tony Raymond points out the advantages of such an arrangement.

The Open University, he says, is the only university without a library and the students cannot make use of any other university library. An association between the university and the Royal Institution would, for one thing, provide library facilities and it would also give students the opportunity to attend outside lectures. The events of the BA could also be attended if there was an association with it.

Mr Raymond has already approached both the bodies concerned and the response has been encouraging. A spokesman for the BA said this week that the association was interested in cooperating with any person or body that was involved in science and technology and that included the Open University.

But at this stage the possibility of links is strictly at the preliminary stage. The Open University said this week that it was giving Mr Raymond every encouragement but that it was taking no official action to help him. The next step is to see what sort of response Mr Raymond gets following his open letter to the students asking them whether they are interested in a close association with these bodies.

Perhaps the most important aspect of Mr Raymond's letter is his highlighting of the anomalous position of Open University students when they apply for membership of professional institutions. Most professional bodies have a class of membership for students but such membership usually has a basic educational requirement and an age limit, both of which most Open University students fail to satisfy.

NEW WORLD

NASA-Style Plan For Cancer Research

by our Washington Correspondent

PART of the much delayed and highly controversial National Cancer Program plan has at last seen the light of day A blueprint for cancer research in the United States for the next five years, the plan was ceremonially handed over to President Nixon last week along with two other reports on progress in the much publicized crusade against cancer It is a remarkable document in many respects, not least of which is that it represents a unique approach to the planning of scientific research, and it is sure to add fresh impetus to the growing debate about whether centrally directed, NASA-style management of cancer research is either timely or productive

The fruit of some forty planning sessions involving 250 scientists which took place between October 1971 and March 1972, the plan was ultimately put together by officials of the National Cancer Institute (NCI) For some six months it has been bogged down in reviews chiefly by the Office of Management and Budget The portion released last week, called the Strategic Plan, is a systems analysis approach to the management and organization of cancer research, setting out objectives, major courses of action and estimates of the resources that will be required for the cancer crusade in the next five years The second part of the plan, the so-called Operating Plan, will be rather more interesting, for it will set out specific programmes to be funded and alternative ways of allocating the resources But the operating plan will not be ready for another year and even then it will be distributed only to those responsible for managing the Cancer Program

The strategic plan describes itself as a disease-orientated approach to the administration of cancer research To achieve the ultimate goal of developing "the means to reduce the incidence, morbidity and mortality of cancer in humans" The plan sets out seven major objectives ranging from prevention to rehabilitation The objectives are then defined in terms of "approaches"—for example, "reduce development of cancer by altering immunological capability of individuals" — and these are further broken down into "approach elements" and "project areas", which is where actual research projects fit into the picture The plan, simplified into a diagram with the goal at the centre and the objectives radiating from it like spokes of a wheel, has been hanging on some laboratory walls at the NIH campus in Bethesda for several months where it has been treated with various degrees of respect and has even been found to make a good dart board

While it is no small feat to assess the staggering amount of research bearing on cancer and to set out an overall set of goals and strategies, the tricky and more controversial questions of how much money should be devoted to individual projects or different approaches, is not spelled out in the strategic plan unveiled last week—those questions will be tackled in the operating plan, which is one reason why it is not yet ready But the Strategic Plan does give estimates of the total resources that will be required for the cancer crusade in the next five years

By 1978, the plan would require some $1,200 million to be spent on cancer research in the United States, of which about $850 million would be provided by the National Cancer Institute (The rest would come from other Institutes of the National Institutes of Health, State and Local Governments and volunteer organizations) That total compares with about $512 million spent in 1971 As for the NCI itself, the plan suggests that its budget for the 1974 fiscal year (which started on July 1) should be $500 million, in other words, the same amount as the Administration has already requested, and that it should increase steadily over the next five years by an average of about $65 million a year By 1982, the plan envisages that the total cancer crusade will be consuming some $1,700 million a year

As far as manpower is concerned, the plan warns that "the unavailability of required scientific manpower may constrain achievement of the program target operating level" Some 9,300 scientists will be required in 1978 for the portion of the cancer programme operated by the NCI alone, while only about 5,000 scientists are now involved in NCI-supported cancer research Can present training programmes meet the demand? Those who drew up the plan believe not, for they suggest that a "deficiency in the number of scientists continue to increase as the program expands" It should be pointed out, however, that the plan was drawn up before the recent announcement that at least part of the NIH training programme is to be saved from the budgetary axe (see *Nature*, **244**, 128 , 1973)

The plan is sure to generate some criticism about its specific conclusions and recommendations, but it has already sparked considerable controversy over the more fundamental issue of whether or not cancer research is amenable to the systems analysis approach that the plan takes In particular, is the move towards tighter central planning likely to stifle creativity? And is the increasing emphasis on cancer likely to take funds away from equally deserving areas of biomedical research?

Those questions have been raised increasingly in the past few years particularly in regard to the growing use of contracts as opposed to grants to fund biomedical research Many of these were set out in a review of the strategic cancer plan carried out last year by the Institute of Medicine, part of the National Academy of Sciences The institute's review, which has not been made public but which has been extensively leaked, raised objections to some specific points in the plan but criticized it chiefly for leaving the impression that all shots can be called from a central headquarters, that all, or nearly all, of the really important ideas are already at hand, and that given the right kind of administration and organization the hard problems can be solved

The institute suggested that a centrally planned, accelerated research programme may be applicable to a small number of cancers for which therapeutic technology is relatively effective and

Cancer Panel

PRESIDENT NIXON announced last week that he has appointed Dr Ray D Owen, Professor of Biology at California Institute of Technology, to be a member of the President's Cancer Panel A three-member board charged with monitoring the development and execution of the National Cancer Plan, the panel report directly to the President on any blockages or delays in carrying out the programme It is thus an influential body It was also announced that Mr Benno C Schmidt, managing partner of J H Whitney and Co, has been reappointed chairman of the panel for a second term of one year Dr Owen replaced Dr Robert A Good, whose term of office expired on February 22 The third member of the panel is Dr R Lee Clark, director of the M D Anderson Hospital and Tumor Institute in Houston where the direction that research should take is reasonably clear Included in that group are acute childhood lymphatic leukaemia, Hodgkins disease, choriocarcinoma, Wills' tumour, carcinoma of the cervix and some skin carcinomas But for the majority of cancers a NASA style assault may not be the best approach since the way ahead for research is "not at all clear" The institute suggests that research on such cancers "ought to involve rather less in the way of centralization, and rather more of a tendency towards decentralization" The institute puts into a nutshell many of the arguments against strong central planning of basic research

"What is most urgently needed for problems of this kind is an abundance of new ideas and these are most likely to emerge from the imagination of individual scientists it is much less likely that the administrators of large programs, or committees of administrators, at the centre of a highly centralized bureaucracy, can generate the kinds of ideas that are needed"

In particular, the trend towards central control and planning of cancer research has generated two highly controversial issues in the funding of research in the USA The first is a move towards more contract research as opposed to grants (more than 50% of the research supported by the NCI is now accounted for by contracts), and the second is an attack on the peer review system by which NIH grants are funded The two issues are closely intertwined, and they represent considerable change in the operation of biomedical research

The traditional way of determining which research should be funded by NIH is by committees of scientists which examine grant proposals submitted by individual researchers and rate them according to their scientific merit The final funding decision rests with NIH officials, but the peer review mechanism is perhaps the most influential part of the process, and it is jealously guarded A recent memorandum prepared by the Office of Management and Budget suggested, however, that the peer review system "is not readily compatible with targeted research or directed research to achieve specific national objectives", and suggested several ways of "improving" the system, including abolishing it (see *Nature*, **243**, 256 , 1973)

The cancer plan specifically stated, however, that the peer review system will continue to be utilized for review of research proposals submitted by those individuals who wish to apply for support through the grant mechanism But it had little to say about the trend towards contract research, except to point out that "the assessment of contract proposals for scientific merit is as important as grant proposals" One concern is that if contract research continues to grow, it will take money away from investigator-originated research Dr James Watson of Harvard University, recently told a Congressional Committee, for example, that "the forthcoming governmental prescription for cancer research ominously points in the direction of more contract money, in which the individual scientist decides where the future may lie"

Another central question about the crusade against cancer is that it may be swallowing up funds for other areas of biomedical research Such charges, in fact, seem to have some substance since every Institute in NIH except for the National Cancer Institute and the National Heart and Lung Institute suffered budget cuts last year The Institute of Medicine said in its review of the plan, for example, that many areas of basic biology may be crucial to the cancer programme, and pointed out that "it would be a dead loss to the cancer effort if research of this kind were to go without support because of fund shortages in other institutes of NIH"

But the actual level of support recommended for cancer research in the plan is likely to become a controversial issue in itself, aside from the question of whether it is soaking up money from other research

It is suggested in the plan that the NCI should receive $500 mililon next year, which is the same amount as the administration requested But the National Cancer Advisory Board, whose annual report was published last week, recommended that $600 million should be made available Moreover, the plan calls for a budget for the NCI in 1975 of about $600 million but a preliminary budget plan drawn up by Dr Charles C Edwards, the Government's top health official, which was recently leaked to Senator Edward Kennedy, recommends an increase in the NCI's budget of only $25 million That would fall some $75 million short of the level proposed in the plan It is thus likely that the most prominent debate about the cancer programme is how much money it should receive But it is clear that more basic issues are involved

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SKYLAB

Preparing for Kohoutek

by our Washington Correspondent

NASA officials are studying plans to delay launch of the third and final Skylab crew for 10 days in order to get a better look at the comet Kohoutek Predicted to be one of the most interesting and perhaps the most spectacular comets this century, Kohoutek will swing behind the Sun, reaching perihelion (its closest approach to the Sun) on December 28, and will pass closest to the Earth on January 15 Skylab is now set for launch on November 9 and splashdown in the Pacific on January 4, and so a 10-day delay will enable closer study of the comet after its periphelion has passed

The original launch schedule would allow the comet to be studied during its approach to the Sun and for a short time after perihelion But it would miss the period during which the comet will be cooling down, when it so happens that the Earth will be in the best position to view the tail A new ultraviolet camera will probably be added to Skylab's instruments in any case, and the Apollo Telescope Mount will be used to view the comet over a wide spectral range at perihelion

In addition to Skylab, NASA is hoping to look at Kohoutek with instruments aboard several other spacecraft The Orbiting Solar Observatory (OSO-7) will be used to view the comet at perihelion, while OAO-C (Copernicus) will turn its instruments towards Koboutek as the comet approaches and recedes from the Sun (Copernicus cannot turn its instruments and its solar panels towards the Sun at the same time) The Mariner Venus–Mercury spacecraft, which is set for launch on November 3, and the Pioneer spacecraft which are on their way to Jupiter will also be used to study Kohoutek, and in addition NASA is planning to launch sounding rockets and to use high-altitude aircraft There has also been talk of sending an Explorer spacecraft directly into the tail of the comet, but it seems that idea has been shelved because of lack of money, although there is a proposal under consideration to send an Explorer to the Grigg–Skjellerup comet in 1977

One reason for the intense interest in comets is that if they were formed outside the orbit of Neptune, as one widely-held theory suggests, they may consist essentially of primordial solar system material largely unmodified by solar radiation That would be especially true of a long period comet such as Kohoutek, which is reckoned to have an orbital period of several thousand years

A decision on the final Skylab launch date will not be taken until after the present mission is completed, but there is a possibility that the launch, instead of being put back, may have to be brought forward to reduce the length of time that the laboratory will be unmanned , the decision hinges chiefly on an assessment of the condition of the spacecraft at the end of the present mission But if the launch is brought forward, the chance of using Skylab's instruments to observe the comet may be missed entirely

NEWS AND VIEWS

Measuring the Speed of Light More Accurately

WITH the increasing interest in space comunications and in the correlation of optical astronomical data with those obtained by radio astronomy, much effort has recently been devoted to a more accurate measurement of *c*, the velocity of light, which relates wavelength to frequency. Although the present length standard, the krypton-86 605.7 nm visible wavelength standard, has a reproducibility of one part in 10^8, and the present frequency standard, the caesium atomic beam, has a reproducibility of one part in 10^{12}, the value of *c* previously accepted had an accuracy of one part in 10^6.

The reason for this low accuracy compared with that of the length standard, which in principle limits the determination at present to one part in 10^8, is associated with the wavelength of the radiation at which the comparison of frequency and wavelength was carried out. In order to achieve high precision wavelength measurements it is necessary to work at wavelengths of 10 μm or shorter. But at the time when Froome measured *c* at the National Physical Laboratory (*Proc R Soc*, **247**, 109, 1958) it was not possible to measure the frequency of sources in the optimum region, and the measurements were made in the microwave region. In this region the wavelength of the sources is comparable to the dimensions of the interferometer used for the wavelength measurements so that large diffraction corrections are necessary.

Since the earlier experiments were carried out some highly stable laser sources have been developed in the region from 10 μm to 700 nm, and the frequencies of some of these have been measured. The most promising of these sources are the CO_2 lasers oscillating between 9 μm and 11 μm stabilized on a very narrow fluorescence signal from an intracavity passive CO_2 cell, the 3.39 μm helium-neon laser stabilized at the centre of the saturated absorption line of methane, and the 632.8 nm helium-neon laser stabilized on one of the molecular iodine saturated absorption lines which lie under the doppler gain profile. The wavelengths of all of these sources have been measured relative to the length standard and a reproducibility of one part in 10^9 can be obtained once corrections are made for the asymmetry of the krypton emission line (*J Phys E*, **6**, 647, 1973, *Appl Phys Lett*, **22**, 196, 1973, and *Opt Commun*, **6**, 91; 1972). A comparison of the wavelengths of these sources measured in different laboratories shows a reproducibility of the order of one part in 10^9.

In order to measure the frequencies of the sources it is necessary to construct a chain of harmonic coincidences between sources which are suitable for transferring measurements from the caesium standard to the appropriate comparison line. In order to achieve this a set of efficient harmonic mixing devices have had to be developed, principally by Evenson and his collaborators. So far lines of the CO_2 laser and the 3.39 saturated methane line have been measured in this way. The frequency of the 3.39 μm line was measured by Evenson and his colleagues in three stages (*Appl Phys. Lett*, **22**, 192, 1973). In the first stage the frequency of the R10 line of a stabilized 9.3 μm CO_2 laser was measured relative to that of the caesium standard using a harmonic chain involving two klystrons, a 337 μm HCN laser and a 28 μm H_2O laser. In the second stage the frequency of the R30 line of a 10.2 μm CO_2 laser was measured relative to the 9.3 μm line, and in the third stage the frequency of the methane line was measured relative to that of the 10.2 μm line. On page 504 of this edition of *Nature*, Blaney *et al* report the absolute frequency measurement of the R(12) transition of CO_2 at 9.3 μm. Used in conjunction with the R(12)−R(10) difference frequency recently determined at the National Bureau of Standards, the agreement with the frequency of the R(10) line used in the velocity of light experiment is within three parts in 10^{10}. This reproducibility is a good test of the accuracy of this method of frequency measurement.

It is possible that in the future either the 3.39 μm saturated methane line or one of the 632.8 nm saturated iodine lines may become the new length standard, since both lines are sharper and probably more symmetrical than krypton 86, and seem to have a reproducibility of the order of one part in 10^9. This would allow the velocity of light to be defined to an accuracy of one part in 10^9, which is the limit set by the present determination of the alternative length standards.

From a Correspondent

MUSCULAR DYSTROPHY

Blood Cell Abnormality?

from a Correspondent

MYOTONIC muscular dystrophy (dystrophia myotonica) is a disorder of autosomal dominant inheritance, characterized clinically by progressive weakness of distal limb, facial and neck muscles, which usually first becomes manifest in adolescence or early adult life and is slowly progressive, leading as a rule to severe disability in middle life and to death well before the normal age. The phenomenon of myotonia is seen most readily in the tongue and in forearm muscles and is usually easily recognized both clinically and electromyographically.

It has been well known for many years that the disease is not one which is limited to the voluntary musculature, for constant abnormalities in affected patients include frontal baldness (in the male), testicular atrophy, cardiomyopathy, malformation of cranial bones, disturbances of smooth muscle motility, cataracts and extrathyroid hypometabolism. Although many patients demonstrate abnormal glucose tolerance with enhanced serum insulin levels and hypercatabolism of immunoglobulin, no constant or specific generalized metabolic defect has yet been demonstrated. A muscle membrane defect has been postulated to account for the myotonia and perhaps also for the progressive muscular weakness (Denny-Brown and Nevin, *Brain*, **64**, 1, 1941, and Landau, *Neurology, Minneap*, **2**, 369, 1952), but McComas and Mrozek found (*J Neurol Neurosurg Psychiat*, **34**, 441, 1968) that although the resting membrane potential of many muscle fibres was reduced in patients suffering from the disease, the impedance of the muscle fibre membrane appeared to be normal. McComas, Campbell and Sica suggested (*J Neurol Neurosurg Psychiat*, **34**, 132, 1971) that as the disease progresses, there is an increasing loss of motor units in the extensor digitorum brevis muscle of the foot and they postulated a primary defect of motor innervation. Histochemical studies of muscle biopsies from such patients have shown a consistent atrophy of type I (slow-twitch, oxidative enzyme-rich) muscle fibres (Engel, *Proc. Int. Congr. Neurol., Vienna*, **2**, 67; 1965).

Now for the first time a study by Roses and Appel (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 1855; 1973) has suggested that in such patients there may be a consistent and reproducible metabolic abnormality demonstrated in erythrocyte membranes or "ghosts". They prepared the erythrocyte ghosts from blood samples obtained from fasting patients with myotonic muscular dystrophy and compared their findings in these individuals with those obtained on similar samples derived from control subjects matched for age and sex. When the ghosts were incubated with [γ-^{32}P] ATP, there was no significant difference in the degree of labelling of ghost proteins if fresh preparations were used. But when the experiments were carried out after storing the ghosts at −20° C for 7 days the incorporation of ^{32}P in the controls was twice as high as in fresh preparations, whereas that in the myotonic ghosts was unchanged and was now significantly less than the controls. On the other hand, freezing in dry ice and thawing immediately increased phosphorylation in both groups, with no significant difference between them. No differences could be demonstrated in phospholipids, gangliosides or sialoproteins or in the membrane polypeptide electrophoretic profiles with control and myotonic ghost preparations.

The diminution in endogenous erythrocyte protein kinase was not likely to be attributable to differences in substrate, because the K_m for ATP was identical and the polypeptides to be phosphorylated were electrophoretically identical in normal and myotonic preparations. The ability of acute frozen erythrocyte polypeptides from myotonic patients to be phosphorylated at twice the rate for fresh or aged frozen preparations also suggests that the amounts of protein substrate were not responsible for the differences noted in enzyme activity. As the authors comment, it is unclear whether the lower than normal protein kinase activity which they found in 7-day frozen myotonic preparations was the result of an intrinsic change in enzyme protein or of a change in the state of the membrane associated with a less stable configuration of the enzyme protein, or to an altered reactivity with its specific substrates.

These results are difficult to interpret, but suggest that there may be a specific structural or metabolic abnormality in the circulating red blood cells in patients with myotonic dystrophy which, if it can be confirmed, demands further investigation. Clearly more work is now required on membrane-bound protein kinase in muscle tissue and further studies are needed to characterize and extend these observations relating to the involvement of the erythrocyte membrane in this disease process.

MEMBRANES

Phases for Ases

from our Molecular Biology Correspondent

SINCE Danielli brought the tablets down from the mountain, the membrane field has come close to being engulfed by such a rapidly swelling flood of information about the phospholipid bilayer that biochemists might do well to head for the hills. There is scarcely a physical technique that has not been pressed into service, be it X-ray diffraction, Raman spectroscopy, calorimetry, ESR, proton, deuteron, carbon, nitrogen or phosphorous NMR — but enough; for the question remains whether the welter of facts, phenomena and conjecture leads to any coherent picture of how membranes actually perform their physiological tasks, in particular selective transport of solutes. For all that is known about the behaviour of lipids and phospholipids in membranes and models, there is an enduring dearth of hard information about how this relates to the structure and activity of the proteins embedded in them, which among other things are the agents of transport.

The most interesting evidence of a direct relation between enzymatic activity and the physical nature of the bilayer comes from comparisons of the effects of temperature on both. It is well established that real and artificial membranes undergo a profound change in character at a critical temperature, the value of which depends on the lipid composition. Above this temperature the membrane is essentially disordered, with rapid rotational and translational diffusion of lipid molecules in the plane of the bilayer, and uninhibited mobility of the hydrocarbon chains towards the centre. Below the critical temperature the structure is essentially frozen into a hexagonal lattice, the hydrocarbon chains being tightly packed in the all-*trans* configuration. The critical temperature may therefore properly be regarded as marking an order-disorder phase transition.

In membranes that contain lipids with *cis* ethylenic bonds, the ordered state is destabilized, the transition temperature is lowered and the discovery of bacterial auxotrophs for unsaturated fatty acids has therefore made it possible to vary the critical temperature of *Escherichia coli* membranes almost at will. Overath and Trauble (*Biochemistry*, **12**, 2625; 1973) describe the properties of cells grown in the presence of different *cis* and *trans* monounsaturated fatty acids. They show that the thermal phase transition can be observed by a variety of simple methods, such as dilatometry, turbidimetry and fluorescence of mem-

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mRNA in Health and Disease

Two communications in *Nature New Biology* next Wednesday (August 29) resolve outstanding questions concerning the life history of mRNA in eukaryotic cells. Bryan and Hayashi have posed the question: are proteins bound to mRNAs in eukaryotic cells in general, and, if so, are they the same proteins which are known to be bound to globin mRNA in the same organism? Two proteins—so far characterized only in terms of molecular weight, one, 49,000–52,000, and the other, 73,000–78,000, estimated by polyacrylamide gel electrophoresis in SDS—are known to be associated with globin mRNA. These messenger ribonucleoprotein (RNP) particles are released on the dissociation of reticulocyte polysomes into subunits.

Bryan and Hayashi performed similar experiments on pulse-labelled chick embryo cerebral polysomes (salt-washed to remove contaminating proteins) and isolated messenger-containing particles sedimenting in the range of 10–30 S, 50 S and 70–200 S. All three fractions contained two proteins of molecular weights 48,400 and 78,500, estimated by SDS gel electrophoresis. These authors also found that reticulocyte globin mRNP yields proteins of 47,000 and 77,000 in agreement with the earlier work. Bryan and Hayashi cite contemporary published works by Blobel claiming that mRNA of L cells and rat liver polysomes likewise bind proteins of 52,000 and 78,000 molecular weight. The results, taken together, indicate that a wide variety of messengers are associated with two proteins with the same molecular weight distribution. Whether the proteins are identical in different messenger particles can be settled only by more rigorous comparisons.

Hatta *et al.* have traced the deficiency of the β chain of haemoglobin in β-thalassaemic patients back to its origin in the erythroblasts of bone marrow. The question they have resolved is whether the known deficiency in circulating reticulocytes is caused by selective nucleolytic destruction of the β-globin mRNA at an earlier stage, or by reduced synthesis of this mRNA. Deranged control at the level of DNA transcription seems to be the primary cause of β thalassaemia in the case studied by these authors.

brane-soluble dyes. The transition occurs between 40° C for a typical all-*trans* species and 14° C for one containing a *cis*-ethylenic bond. The transition temperature is largely determined by the preponderant membrane lipid, phosphatidylethanolamine. A striking feature emerges once more from the temperature dependence of transport-linked functions, such as hydrolysis of a galactose ester by the cells: when expressed in terms of Arrhenius plots, the hydrolytic rates show two linear phases in all cases, with a sharp discontinuity precisely at the critical temperature, determined by the unsaturated fatty acid made available during cell growth. Thus the activity of the corresponding transport enzyme is inhibited when the lipid phase solidifies.

The demonstration of how the composition of the bilayer relates to the membrane assembly process represents a noteworthy advance in linking its physical properties to function. Tsukagoshi and Fox (*ibid.*, 2816), following their earlier observation that different transport processes, based on unrelated enzyme systems, evince a change of activity at the same critical temperature, have now shown that induction of the lactose transport system in *E. coli*, measured by levels of enzymatic activity, fails below a critical temperature, which is again identical to that of the lipid phase transition, and depends accordingly on the nature of the fatty acid supplement. Tsukagoshi and Fox (*ibid.*, 2822) go on to show that the transition temperature for transport activity can be progressively varied by switching from one fatty acid to another during growth, if the temperature is above critical. If the transport system is induced at a temperature below the critical after switching from one fatty acid to the other, a new phenomenon supervenes: the Arrhenius plot shows three phases. The second discontinuity can be eliminated by, as it were, annealing the cells above the transition temperature. The inference is that below the bilayer melting temperature, the transport enzymes are insinuated into the membrane in their own pool of freshly synthesized lipid. If this is of a type associated with a high melting temperature, then these ice-floes will survive after the rest of the membrane, with its own population of enzymes has melted, to melt ultimately at their own characteristic temperature. When the growth temperature is above critical the new lipids which result from the fatty acid switch will simply be dispersed in the fluid membrane, along with the induced enzyme, and the critical temperature will simply reflect the average composition.

The dependence of the activity of a transport enzyme on the fluidity of the bilayer has also now been demonstrated in an animal system. Grisham and Barnett (*ibid.*, 2635) find that at 20° C the activation energy of the sodium-potassium ATPase of outer kidney membrane undergoes a twofold change, and at the very same temperature the signal from a spin label in the membrane manifests a convulsion. These experiments were done on a complex of the enzyme with its characteristic complement of lipids. When these are extracted from the preparation and examined as a protein-free bilayer, they show the same phase change, from which it follows that it is the lipid that controls the state of the enzyme, not the converse. Grisham and Barnett also show that the lipid environment of the enzyme is appreciably different from that of the membrane as a whole, for spin labels on long fatty acid esters, that project deep into the bilayer record greater fluidity in the purified ATPase membrane, whereas a label closer to the head groups, no mobility difference is in evidence. Similar breaks in the Arrhenius plots for two enzymes in microsomal membranes have been observed by Eletr, Zakim and Vessey (*J. Molec. Biol.*, **78**, 351 , 1973). Comparison with phase transitions in the bilayer, recorded by spin labels, before and after sonication and following phospholipase treatment, indicates that the two enzymes are surrounded by atmospheres of phospholipid differing appreciably in composition.

One of the most rewarding areas—

Forever Blowing Bubbles

Two novel communications, one theoretical and one experimental, on the mechanism of DNA replication appear in *Nature New Biology* next Wednesday (August 29). The theoretical paper by Ioannou proposes a general model to account for all the known facts about DNA replication ; Hobom and Hobom present experimental evidence for a model for λ*dv* replication, which appears to be an exception to the rule that RNA is necessarily involved in DNA replication.

Ioannou's model of DNA replication contains the following essential points. DNA replication is based on units of replication which he calls "unitrons", of which there are many, separated by variable distances in different DNA species. After two breaks in the DNA at opposite ends of the unitron, an RNA complement of the two free 3′ ends, consisting of about fifty ribonucleotides, is made. This RNA–DNA hybrid serves as a primer for the synthesis of DNA complementary to the remaining single strands of DNA in the unitron. The resultant four stranded structure is called a "microbubble". The RNA is then excised, and according to the model, the microbubbles condense to form "macrobubbles". The single stranded DNA corresponding to the previously stable double stranded regions of about 100–200 nucleotides long is then copied by the normal repair mechanism and the nascent DNA segments are joined by DNA ligase.

The model is consistent with many known features of DNA synthesis. Unidirectional replication would require an impossible rate of unwinding DNA, about 10,000 r.p.m. Multiple sites for DNA initiation have been found in replication systems of phages, prokaryotes and eukaryotes. Macrobubbles have been observed by electron microscopy and autoradiography. The model is consistent with the size of Okazaki fragments, known intermediates of DNA synthesis. An RNA primer is known to be universally involved in DNA synthesis in viruses, bacteria and higher organisms. Inhibitors of RNA synthesis, rifampicin and streptolydigin, inhibit only the initiation of DNA replication.

The model is elaborated to demand, generally, a two-fold rotational axis of symmetry perpendicular to the helix axis at each end of the unitron. Such regions are known to be common in DNA. DNA unwinding enzymes have been characterized in a number of systems. The RNA primer could be removed exonucleolytically either by RNase H or DNA polymerase I. The growth of macrobubbles may depend on cytoplasmic factors accounting for bidirectional and unidirectional DNA synthesis observed at the replicating forks of DNA.

Hobom and Hobom accept the idea that an RNA primer is generally required for DNA synthesis, but seem to have found an exception to the case in the replication of λ*dr* DNA. Their evidence is based on the resistance of replication of this mutant to inhibitors by rifampicin. They propose an alternative model for DNA replication which is possible owing to the special structure of λ*dv* DNA. According to their model the DNA is present as a dimer replicon with two origins of replication opposite each other on a circular DNA molecule. Bidirectional replication of λ*dv* starting at the end of one or other of the origins is predicted to lead to termination reactrons localized on the DNA molecule very close to the second site of origin. They suggest that the remnants of these reactions—short pieces of DNA strands—may be re-usable for priming the next round of initiation at this second site of origin.

in more senses than one—in the study of membranes just now concerns transformed cells in tissue culture, which as all the world knows show enhanced agglutinability by lectins Noonan and Burger (*J Biol Chem*, **248**, 4286, 1973), aside from showing that the phenomenon is not only (as has been suggested) the result of greater membrane fluidity, but also of a greater number of available binding sites, have demonstrated a precipitous change in the amount of concanavalin A bound at 15° C, which again is a manifestation of a bilayer phase transition

For students of the tricks of bilayers, Michaelson, Horwitz and Klein (*Biochemistry*, **12**, 2637, 1973), have demonstrated a tendency of particular phospholipids to collect preferentially on the inside or outside surface of vesicles, according to their ionic nature, and McNamee and McConell (*ibid*, 2951) have found that in electroplax membrane vesicles there is a continuous migration of phospholipids back and forth between the inner and outer surface on a time scale of a few minutes at 15° C

LOCUSTS

Pheromone Identified

from a Correspondent

PHASE transformation in locusts refers to the changes induced when solitary hoppers (juvenile locusts) become gregarious The process is reversible in the instar stages because it is dependent upon the insect's population density Gregaria hoppers are more active, need more food and are darker in colour than the solitaria hoppers (the latter are a green to fawn colour), and the gregaria adults assume longer wings and broader heads than their solitary counterparts There is, however, one feature of the gregaria phase that can be measured more accurately than behavioural and physiological phenomena, during meiosis in the swarming adult male, the frequency of chiasmata (genetic crossing over) is increased as much as 30% over that of solitary males (Nolte, *Chromosoma*, **21**, 123, 1967)

Chemical communication plays a dominant part in the behaviour of locusts In the desert locust, *Schistocerca gregaria*, olfactory information is important for food seeking, for synchronizing maturation, and for localizing oviposition It was on this basis that Nolte (*Nature*, **200**, 660, 1963) postulated the liberation of a pheromone (a substance secreted to the outside of an individual and received by a second individual of the same species, in which it releases a specific action) by massed locusts that would trigger off gregarization processes Nolte *et al* (*Chromosoma*, **29**, 462, 1970) later found that the postulated pheromone was excreted in the faeces of solitary and gregarious hoppers (but not of the adults) The production of the pheromone was found to be related to the crop section of the alimentary tract and perception of such a stimulus appeared to be through the spiracles directly into the haemolymph

Nolte *et al* (*J Insect Physiol*, **19**, 1547, 1973) have now obtained evidence that this pheromone is 2-methoxy-5-ethylphenol, a derivative of guaiacol, which is a degradation product of the metabolism of the lignin of plants They postulate that lignin is ingested in grass or shrubs and degraded in the crops of the larvae to guaiacol, some of which is excreted in the faeces, and the rest changed to the active pheromone (called "locustol") and also excreted

The pheromone and some other substances were extracted by steam distillation and pentane extraction of hopper faeces Gas chromatography of the pentane extract and preparative thin-layer chromatography of a more intensely purified extract disclosed two major and several minor components Mass and nuclear magnetic resonance spectroscopy suggested that the two major substances are guaiacol (O-methoxyphenol) and 2-methoxy-5-ethylphenol, and this was confirmed by comparison of the effects of the two extracts and the two synthesized suspected compounds (and some of their isomers) on gregarization

Four characteristics of gregarization in *Locusta migratoria migratorioides* were used in the identification of the pheromone colour change during the various instars, chiasma frequencies during the first few days after becoming adult, adult morphometric ratios, and behavioural traits Chiasma frequencies of the eight largest autosomes (the three shortest invariably exhibit one chiasma per pair) provided the most sensitive index of gregarization Of the other criteria involved, pigmentation is influenced by other external factors (for example, humidity) as well as by chemicals, morphometric ratios are somewhat restrained under laboratory conditions and behaviour is difficult to standardize

Considering these four criteria, locustol was shown to be the most active constituent of hopper faeces, although several other substances were shown to possess varying degrees of activity on one or more of the gregarization traits Thus in a congregating group of hoppers gregarization will be triggered off by the accumulation of locustol in the atmosphere around the group Previously, gregarization was found not to be so prominent a phenomenon in well ventilated laboratories The ecological significance therefore in field conditions of a phenomenon that seems to depend on the build-up of a substance in a confined space has yet to be assessed

SOLID STATE PHYSICS

Energetic Phonons

from our Condensed Matter Correspondent

IN a recent issue of *Physical Review Letters* (**31**, 215, 1973) Welte and Eisenmenger of Stuttgart University report that they have succeeded in generating extremely energetic phonons, with frequencies v in the region of 1 THz (10^{12} Hz), by using superconducting aluminium tunnel diodes

The thermal energy of a crystalline solid takes the form of quantized lattice vibrations, known as phonons From the thermodynamic point of view, a simple solid may be regarded as an empty box containing a large number of phonons, each of energy hv, behaving very much like a gas of rapidly moving free particles Phonons of low frequency and energy travel at the velocity of sound Their velocity falls with increasing frequency until, at the so-called Debye cutoff frequency v_D, which is characteristic of the material, their velocity becomes zero Phonons of frequency greater than v_D are not a very meaningful concept since they would have wavelengths shorter than the interatomic spacing

At high temperatures the mean free path λ of the phonons is very short because phonon-phonon collisions are frequent But at temperatures near 1 K, at which relatively few thermal phonons are present, λ can become comparable with the dimensions of the specimen, this situation is analogous to the molecular flow regime of a low pressure gas A high energy phonon introduced at one end of the specimen has, therefore, a high probability of continuing in a straight line until it strikes a boundary so that, by using a suitable phonon generator and detector, the passage of a pulse of phonons across the specimen can be investigated Unfortunately, conventional techniques for generating phonons are either restricted to relatively low frequencies, much less than v_D, or produce phonons which are not monochromatic but spread over a wide range of frequencies

While working with A H Dayem at the Bell Telephone Laboratories, however, Eisenmenger was able to report in an earlier paper that a superconducting

Correction

As the result of editorial error, Professor J Yvon, of the Commissariat à l'Energie Atomique (CEA) in Paris, was inadvertently described in the News and Views article "Molecular Motions" (*Nature*, **244**, 256, 1973) as coming from the University of Paris, so, too, was Dr P Lallemand, of the École Normale Supérieur tin tunnel diode can be used as a generator of relatively high energy phonons (*Phys. Rev. Lett.*, **18**, 125, 1967). Such a junction consists of a sandwich of two thin layers of superconductor separated by a very thin layer of insulator, and is prepared by evaporating the materials under high vacuum. When a suitable voltage V is applied between the electrodes, electrons are able to "tunnel" through the insulator, and arrive in the positive electrode with an excess energy of eV. It was found that, if the bias voltage was chosen so that eV was greater than twice the energy gap Δ (separating the ordinary electron states from the lower energy, paired, superconducting states) of the tin, most of the injected electrons gave up their excess energy in a two stage process: they fell first to the top of the energy gap by emission of a phonon or phonons whose maximum energy must be $eV-2\Delta$, and then dropped into a paired state with emission of another phonon whose energy was always 2Δ.

The experimental arrangement consisted of a diode formed on the end of a sapphire rod, so that the phonons which were generated could escape and propagate freely in the sapphire. A second diode was used to detect their arrival at the other end of the rod. Unfortunately, it turned out that phonons generated by the first process, known as relaxation phonons, were unable to escape from the diode, being strongly absorbed by the tin and giving rise, ultimately to further phonons of energy 2Δ, which is a great deal less than $\nu_{\rm D}$ for most materials.

In their latest experiments, the Stuttgart group has been able to show that, for aluminium junctions, the energy of the emitted phonons is not limited to 2Δ, probably because the electron-phonon interaction is smaller than for tin, so that the relaxation phonons have a better chance of escaping.

The phonons were allowed to propagate in a silicon crystal. In order to show convincingly that they really were dealing with phonons of energy up to $eV-2\Delta$, they "doped" the silicon with a little oxygen, since infrared studies have shown that there is then a very strong resonant absorption of energy at 29 cm^{-1}, and they report that they did indeed observe a phonon absorption line at an energy within 1% of the predicted value, which was at about 24Δ, corresponding to a frequency of 0.87 THz. Forkel *et al.* believe that their technique should enable phonons to be generated right up to the Debye limit of $\nu_{\rm D}=9.5$ THz for aluminium. If they are right, there should follow a whole series of elegant experiments designed to investigate the behaviour of very high energy phonons in a variety of different materials.

PALAEOMAGNETISM

Misidentified Dyke

from our Geomagnetism Correspondent

IT is a long time since palaeomagnetism surprised most of the geological community by giving the first convincing quantitative evidence in favour of continental drift and thus setting the scene for the new global tectonics. But it can still come up with a geological surprise, albeit a more minor one, from time to time, even in a country as much studied geologically as Britain. Much of the more obvious geology of Britain was investigated in detail during the nineteenth and early twentieth centuries, of course; but it would appear from recent work that even its well and long established tenets are not necessarily immune to the onslaught of modern techniques.

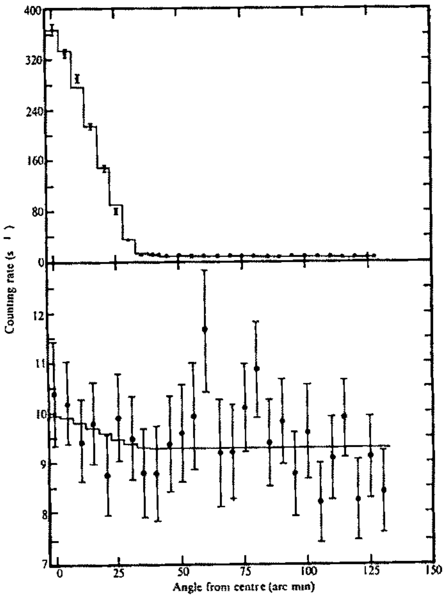
Consider, for example, the Wackerfield Dyke near Staindrop in County Durham, which was studied in detail many years ago by Holmes and Smith (*Durham Geol. Mag.*, **58**, 440; 1921). Although this roughly WNW-trending dyke is not exposed continuously, it is fairly obvious from field relations that it forms part of the Cleveland-Armathwaite Dyke. The latter, in turn, is part of the Eocene Mull Dyke Swarm which, though intense in western Scotland, thins out across southern Scotland and northern England into a much smaller number of larger dykes. Northern England, however, also contains an earlier generation of basic dykes and sills exemplified by the Upper Carboniferous Whin Sill, a system of transgressive quartz dolerite sheets which are intermittently exposed. Generally speaking, the Whin Sill and associated exposures do not follow the clear WNW trend of the Mull Dyke Swarm extension, although, being more erratic in direction, some of the exposures near the Cleveland-Armathwaite Dyke do lie roughly WNW. In spite of this superficial confusion, however, the Wackerfield Dyke has always been regarded as part of the Tertiary activity.

But Tarling *et al.* (*Earth planet. Sci. Lett.*, **18**, 427; 1973) have now used palaeomagnetic and isotopic dating techniques to show that this long-cherished belief must be discarded. The critical palaeomagnetic data come from fresh, unweathered samples of the Wackerfield Dyke exposed by quarrying, although comparative tests were also carried out on samples from the zone of surface weathering. Both thermal and alternating field demagnetization tests show that the natural remanent magnetizations of the fresh samples are extremely stable, and this is confirmed indirectly by the petrology. In the fresh samples, titano-

Are There Two Kinds of Radio Star?

IT is not long since the discovery of a radio source associated with a star ranked as an event of major importance in astronomy. Now, however, several such associations are known, and astronomers have moved on to the next stage in studying these objects—trying to find family relationships between them. The numbers are still too small for satisfactory statistical analysis; but it does now look, according to Bahcall and Kellogg, as if there are two kinds of radio source associated with binary systems, one of which is a strong X-ray source and the other of which is not (see *Nature Physical Science* next Monday, August 27).

Perhaps it would be misleading to call these two kinds of source "classes", however, for of seven systems described by Bahcall and Kellogg six fall in one category and the other, HDE226868, stands alone. Although their calculations assume a thermal bremsstrahlung mechanism, the suggestion that there are two types of radio star (cool sources with $T \lesssim 10^7$ K and HDE226868 sources with $T \sim 10^7$ K) is independent of that hypothesis. Some of the differences between the two categories are brought out in the figure, which compares the X-ray emission from Cyg X-1 (top), the X-ray counterpart of HDE226868, with the lack of X-ray emission from RY Scuti (bottom). The possibility that the identification of HDE226868 with Cyg X-1 is wrong remains, of course, but, say Bahcall and Kellogg, "the present weight of evidence is strongly against this suggestion".



X-ray observations from Uhuru of Cyg X-1 (HDE226868, top) and the region of RY Scuti. The lack of X radiation from systems like RY Scuti suggests that these are fundamentally different from HDE226868.

magnetite is oxidized along 110 and 111 planes to thick ilmenite lamellae and contains spinel rods typical of oxidation classes IV or V Thus there can be little doubt that the resulting palaeomagnetic data are reliable

The mean palaeomagnetic direction from the fresh Wackerfield Dyke samples gives an ancient pole at 175° E, 22° N This is only a few degrees from the pole obtained from Whin Sill samples by Storetvedt and Gidskehaug (*Phys Earth planet Int*, **2**, 105 , 1969) but is well removed from the Cleveland-Armathwaite Dyke pole reported by Giddings' (thesis, University of Newcastle upon Tyne, 1969) It is true that Creer *et al* (*Geophys J*, **2**, 306 , 1959) obtained a palaeomagnetic direction from the Whin Sill which differed from the Storetvedt-Gidskehaug direction by 17°—and this makes the situation less clear than it would otherwise have been Storetvedt and Gidskehaug argued, however, that the earlier result could be due to a stable, secondary post-Permian magnetization and noted that their own data agreed with other European data from samples of comparable age

Tarling and his colleagues are clearly reluctant to arbitrate between the two Whin Sill results , but in view of the fact that the earlier direction was obtained from initial natural remanent magnetizations whereas samples used in the more recent study were demagnetized thermally and by alternating field, it is quite fair to say that the Storetvedt-Gidskehaug result is probably the most reliable In any event, the Wackerfield Dyke pole is certainly well removed from the Tertiary Cleveland-Armathwaite Dyke pole, indicating that the Wackerfield Dyke cannot be Tertiary And this is confirmed by a new radiometric age of 303 ± 5 million years of the Wackerfield Dyke Tarling *et al* thus conclude that, contrary to traditional belief, the Wackerfield Dyke is closely related to the Whin Sill How many more such features remain wrongly identified?

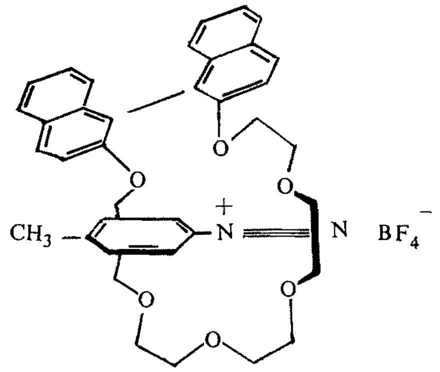
CHEMISTRY

Round Peg in Round Hole

from our Chemical Physics Correspondent

CHEMISTS have for many years been intrigued with molecules of simple but unusual shapes, and examples of boats, chairs, crowns, sandwiches and so on are well known So too are the solid clathrate materials in which guest molecules are held prisoner in a three-dimensional cage of the host, most often hydroquinone Now Gokel and Cram (*J Chem Soc Chem Commun*, 481 , 1973) have provided an example of what may best be described as a peg in a hole, which forms in solution

They find that a solution of 1 mol of the crown-shaped molecule binaphtho-[20]crown-6-cyclic ether in chloroform will dissolve at least 0 9 mol of the peg, *p*-toluenediazonium tetrafluoroborate This they attribute to the formation of the structure in the diagram The solubility is indicative of some complex formation since the diazonium salt is normally insoluble in chloroform



The proposed shape of the complex is supported by the finding that the slight modification of the crown to an open chain form destroys this unusual solubilizing ability The structure is further supported by nuclear magnetic resonance findings The uncomplexed crown molecule has four particular hydrogens in the two Ar–O–CH$_2$– fragments, which are equivalent, or more strictly isochronous, and give rise to a set of lines due to spin-spin coupling that are all based on a single chemical shift, 4 06 p p m When the diazonium salt is also dissolved these lines separate into two sets with chemical shifts of 3 89 and 4 06 p p m , showing that the protons are no longer all equivalent The structure shown predicts this, as two of the protons are on the same side of the crown as the tolyl group and the other on the same side as the BF$_4^-$ ion The fact that the new spin-spin pattern is sharp implies that an individual peg must remain in its own hole for at least a second

At first sight this set of plugged holes floating in the bathwater may seem to be only a curiosity But it has already been shown that the efficiency of the solubilization process is a sharp function of ring size and peg shape, so that quite sophisticated fractional extractions might be possible

Magnetic Properties of Exposed Oceanic Crust

IN spite of the important part played by oceanic magnetic anomalies in global tectonic theory, the nature and form of the magnetic source or sources in oceanic layer 2 remain obscure But a little experimental evidence is available For example, Marshall and Cox (*Bull geol Soc Am*, **82**, 537 , 1971) recently showed that a layer of extrusive rock (pillow lava) less than 1 km thick could account for observed anomaly amplitudes if the high intensity natural remanent magnetizations (NRMs) found in their dredged samples were to obtain throughout the layer High NRM intensities have also been found in samples of pillow lava dredged from the mid-Atlantic ridge, although the reduction in anomaly amplitude away from ridges suggests that high intensities are not universal, possibly because pillow lavas easily undergo low temperature oxidation Lower NRM intensities in older oceanic crust have also been observed directly by drilling into layer 2

But this is only touching the surface, both literally and figuratively — what is really required to solve the problem is the ability to drill right through the oceanic crust, or at least through layer 2 Such complete sampling is, not yet feasible for the present oceanic crust but is possible for formations such as the Troodos ophiolite complex of Cyprus which are thought to be upthrust sections of ancient oceanic crust Another example is Macquarie Island which was almost certainly formed during the late Tertiary at the active Australia–Antarctica ridge , and as Butler and Banerjee showed in last Monday's *Nature Physical Science* (August 20), ancient oceanic crust such as Macquarie Island can have magnetic properties quite different from those of young dredged samples

The Macquarie materials investigated by Butler and Banerjee included pillow lavas, basaltic and doleritic dykes, gabbro and serpentinized harzburgite The first important point to emerge from the study was that the pillow lavas had NRM intensities at least an order of magnitude lower than those of young pillow lavas Their stability to alternating field demagnetization was also lower These results are entirely consistent with the view that pillow lavas gradually undergo low temperature oxidation or low grade metamorphism , but whatever the cause of the lower NRM intensities, it is clear that the contribution to the observed anomalies from pillow lavas must decrease with age

The basaltic and doleritic dykes, on the other hand, were found to be much more stable magnetically than the lavas , and their NRM intensities were high enough to suggest that they may make a significant contribution to the observed anomalies Moreover, even the gabbro and ultramafic intrusive layer cannot be entirely rejected as a magnetic source, for the gabbro has an unusually high NRM intensity and stability for an intrusive rock. In short, "the ability to produce magnetic anomalies is not limited to the pillow lava layer".

Organic Ionic Melts

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Professor Ubbelohde describes recent work on a novel class of liquids—organic molten salts.

TRADITIONALLY, work on the liquid state has dealt mostly with molecules whose repulsive and attractive forces are short range. Even computer models overemphasize "hard sphere" short range forces in the liquid state. Yet when liquids are considered by reference to the types of crystal compound from which they are formed on melting[1], more than one novel class of liquid warrants special attention. As one example, liquids with long range forces between the molecule include many molten salts. With inorganic molten salts, the physical chemistry is becoming better known, and for several years, I have endeavoured to enlarge this class of liquids to include organic molten salts. These have the theoretical attraction that a family of salts might be studied, for example, with a structurally related series of acids in which there are only small differences of structure. This might permit sensitive tests of various theoretical aspects of the liquid state.

One serious and quite general difficulty had to be overcome at the outset of work on organic molten salts. Many of these are relatively stable in crystalline form, but even when their melting points are low and the organic structures simple, it was surprising that the liquids obtained on melting often showed much enhanced chemical instability.

At first, it was not known if this general finding might be due to intrinsic changes in the micro-environment of the ions on passing from the crystal lattice to the molten state[2]. Alternatively, greater instability of the melts might arise from impurities whose molecular freedom of movement is enhanced in the liquid. Recent reaction kinetic studies in organic ionic melts have revealed many suggestive features in favour of the second possibility, and have shown that by carefully excluding certain impurities[3–5] crystalline salts can be prepared that give organic ionic melts indefinitely stable up to about 350° C. These novel liquids are now available for precise studies, as well as for bulk uses, for example in engineering or optical applications.

Some novel aspects may be illustrated by reference to alkane carboxylates with one of the cations Li, Na, K, Rb or Cs. Acid anions of general formula $C_nH_{2n+1}CO_2^-$ were chosen with $n \leqslant 6$ to concentrate attention on organic ionic melts in which the ratio of the charge to the total number of atoms is still quite large, leading to characteristic ionic liquids in which the electrostriction is still high. Many other kinds of organic ionic melts with less electrostriction can, of course, also be studied.

Two-stage Melting

Transition to a "liquid" on melting a "crystal" can be characterized either by thermodynamic or non-thermodynamic (such as mechanical) criteria[1]. With crystals of complex structure, "melting points" defined in these alternative ways may show significant discrepancies. Usually, it is best to identify melting points thermodynamically.

With others, I have determined stable liquid ranges for this novel class of liquids using a scanning calorimeter[6], as well as dilatometry[7,8]. For all five alkali cations, salts with anions up to $n=3$ give conventional ionic melts with a useful liquid range, seldom less than 100° C. But for $n>3$, a novel feature appears, in that a first melting transition occurs at T_f to a mesophase birefringent state. Organic ionic melt mesophases resemble more familiar "liquid crystals" of organic chemistry, except for the stronger and longer range electrostatic forces acting between their molecules. When an organic ionic crystal gives a mesophase at T_f, it passes into a clear ionic melt at higher temperatures (T_{cl}).

Mechanical Mechanisms of Melting

As an alternative to thermodynamic descriptions, a liquid is sometimes defined mechanically as a condensed state of matter incapable of withstanding applied shear stress. On this basis, our recent studies suggest that organic ionic melt mesophases are probably better described as extremely plastic solids, with elastic limits so low that they would be missed in conventional observations. For shear stresses exceeding these limits, once flow starts, mechanical properties may alter because of molecular orientation induced by flow. To study this kind of memory effect, a relaxometer has been designed and constructed in which the forces applied can be as low as 30 nN with sheer stresses as low as 0.1 nN m^{-2}. Although still in early stages of design, this instrument[9] confirms very low elastic thresholds, passing into continuous flow above about 55 nN m^{-2}. Although flow is not strictly Newtonian, viscosities, measured in conventional capillary viscometers, are about 100 poise for sodium-*n*-isovalerate in its mesophase, dropping to about 0.1 poise above the second melting point, T_{cl}.

Texture and Properties

For characteristic examples of these crystals, entropies of fusion are below 3 e.u. and the jump in electrical conductance on melting is exceptionally small[6]. These pointers to a close similarity of molecular arrangements in crystals and melts are confirmed by optical and X-ray studies[10]. Optical studies of birefringence indicate relatively large domains extending over 100 μm in molten sodium-*n*-butyrate and over a few millimetres in molten sodium isovalerate. X-ray measurements over a range of temperatures traversing the first melting point T_f and the second melting point T_{cl} show that these domains contain stacks of parallelized electrostatic sandwiches rather like striped serpents (Fig. 1*b*). Single electrostatic sandwiches (Fig. 1*a*) are formed by pairs of alkane carboxylate layers in opposition.

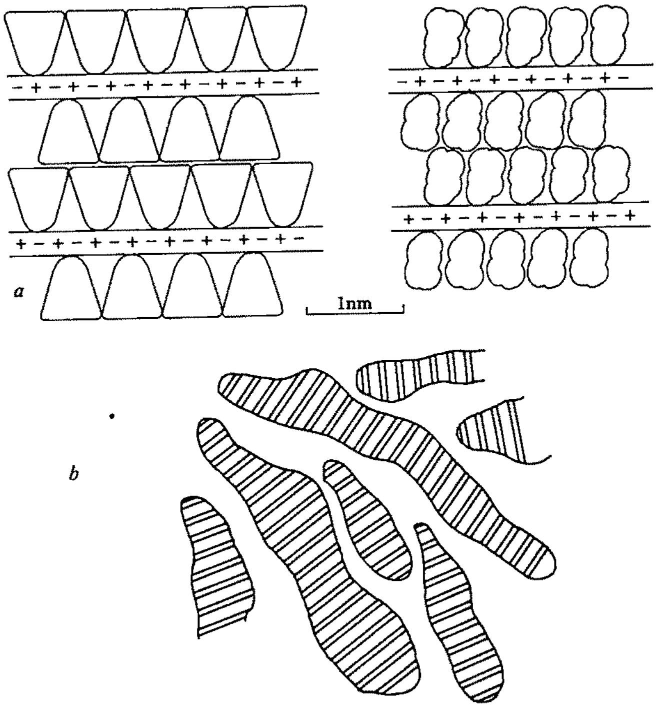

Fig. 1 a, Scale diagram of space occupied by anions (repulsion envelopes) packed between cation (+) and carboxyl (−) electrostatic sandwiches Left, sodium butyrate, right, sodium isovalerate b, Domains of stacked electrostatic sandwiches in organic ionic melt mesophases

In each sandwich, alkane anions are under strong electrostrictive forces from the layers of electrostatic charges This leads to remarkable thermal behaviour as the temperature of the mesophase is raised from T_f to above the clearing temperature T_{cl} In sodium isovalerate, for example, zero thermal expansion is observed normal to the electrostatic layers, over a temperature interval of some eighty degrees, whereas in sodium-*n*-butyrate the electrostatic layers shrink closer together as the temperature is raised. Because the total volume of each of these mesophase melts increases normally with temperature, this implies that the domains (and the more disordered fluid between them) must expand laterally as the temperature rises, up to the clearing point T_{cl} at which the liquid passes into a more normal ionic melt arrangement.

Ionic Melt Liquid Crystals

In recent years interest in molecular "liquid crystals" has flared up to a remarkable extent This has been stimulated by potential technical applications of effects of applied magnetic and electrical fields in optical and other physical properties of these "liquids"[11-15] Preliminary measurements (with J J Duruz) indicate that some of the phenomena already identified with molecular "liquid crystals" take distinctive forms in organic ionic melt mesophases Because these novel ionic fluids have now become available at moderate cost in considerable bulk, the range of "liquid crystal" phenomena which can now be studied in the laboratory and possibly used for practical applications has been considerably extended

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Sensitivity in the World Dynamics Model

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A computer analysis of Forrester's World Dynamics Model shows that the model is very sensitive to the input assumptions with respect to capital investment and pollution. An algebraic description of the model and six considerations basic to such a simulation are also presented.

I SHALL try to illuminate the extensive discussion of Forrester's simulation of the world[1-3] in three ways , by giving a description of the World Dynamics Model in standard algebraic notation rather than the specialized Dynamo notation, by presenting the results of a sensitivity analysis of the model, and by noting some of the fundamental considerations inherent in this kind of simulation

I find that the World Dynamics Model is very sensitive to the input assumptions the change of any one of several values produces large changes in the curves of population, pollution and natural resources These results point in one of three directions either the world is indeed sensitive to small changes in the input descriptors , or the World Dynamics Model is basically a correct description of the world, but it requires a more accurate set of inputs (Tables and constants) , or the model has serious flaws and requires extensive re-examination

Logic of the Model

The World Dynamics Model is a program written in the Dynamo language I describe the program in algebraic notation in the Appendix to this article.

The model is based on two central assumptions , that the world can be adequately described in terms of five state variables (population, capital investment, pollution, agriculture and natural resources), and that these variables, with twelve intermediate ones, can be defined by twenty-two Tables or graphs (see Appendix) The Tables are not based on any statistical analysis (ref 1, chapter 3) , nonetheless, Forrester states that "the model asserts that the relationships chosen for inclusion are important, that the omitted relationships are less important, and the 'real-world' interactions can be represented usefully as described in the details of the model " He goes on to suggest (ref 1, pages 31, 32) that, because of this, "the reader should examine the assumptions and relationships for plausibility and he would want to determine which changes in assumptions result in significant changes in system behavior . "

I have found that "significant changes in system behavior" occur if one point in one of three Tables (CIMT, POLCMT, or POLATT) is changed, if one of two constants (CIGN or CIDN) is changed, or if the growth mechanism in one state variable (population) is modified.

Sensitivity Analysis

I have made more than sixty runs of the World Dynamics Model using the Dynamo compiler and the exact program presented in *World Dynamics*[1] These runs examined three aspects of the model capital investment, pollution, and exponential growth with respect to population

In the Forrester model, the capital investment increment is given by the difference between capital investment generated (CIG) and the capital investment discarded (CID) Thus

$$\mathrm{CI}(t+\Delta t)=\mathrm{CI}(t)+(\mathrm{CIG}-\mathrm{CID})\Delta t \qquad (4)$$

(Equation numbers correspond to those in the Appendix) Capital investment generated is the product of three factors the capital investment generation constant (CIGN), the capital investment multiplier which is a function of mean standard of living, CIMT (MSL), and population, $P(t)$, thus

$$\mathrm{CIG}=\mathrm{CIGN}\ [\mathrm{CIMT}\ (\mathrm{MSL})]P(t) \qquad (2)$$

Capital investment discarded is the product of two factors , the capital investment discard constant (CIDN) and the capital investment [CI(t)] , thus

$$\mathrm{CID}=[\mathrm{CIDN}]\mathrm{CI}(t) \qquad (3)$$

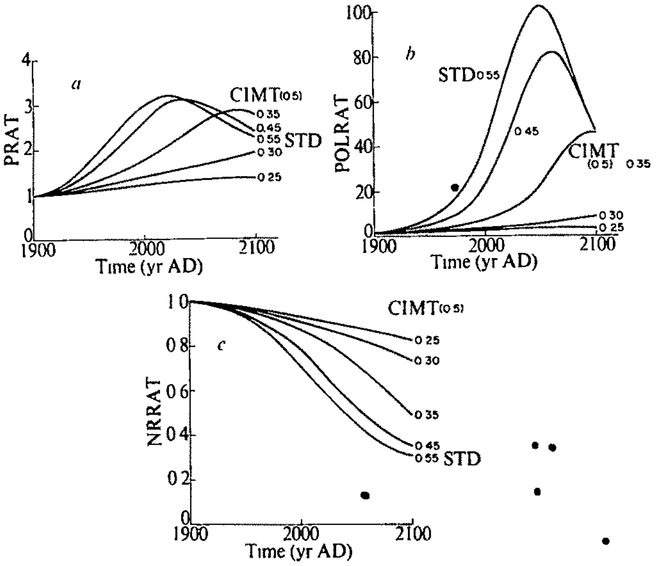

Fig. 1 Effect of varying CIMT (0 5) Time variation of, *a*, normalized population (PRAT), *b*, normalized pollution (POLRAT), *c*, normalized natural resources remaining (NRRAT)

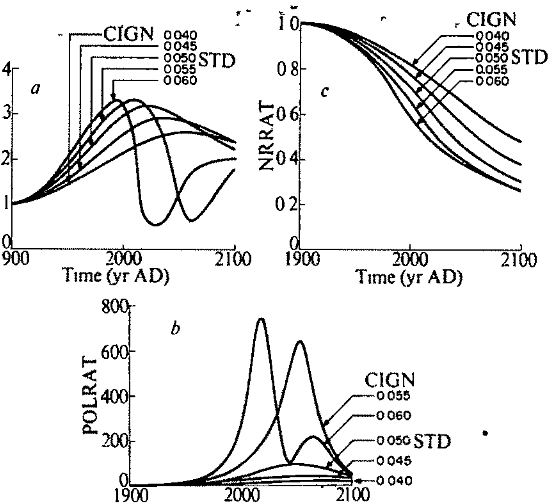

Fig. 2 Effect of varying the capital investment growth normal (CIGN) Time variation of, *a*, normalized population (PRAT), *b*, normalized pollution (POLRAT), *c*, normalized natural resources remaining (NRRAT)

The sensitivity analysis reported here examined the capital investment equations by varying CIMT (0.5) over the range 0 25 (0 05) 0 55 (Fig 1), CIGN over the range 0 040 (0 005) 0 060 (Fig 2), and CIDN over the range 0 015 (0 005) 0 030 (Fig 3)

Each of Figs 1–3 shows relative population, PRAT, relative pollution, POLRAT, and relative natural resources remaining, NRRAT In each case, the variable is the value of relevant state variable at time, t, divided by the state variable value at $t=1900$ Further, in each figure, the curve labelled STD is the one produced by the exact program presented in ref 1

Briefly, as one point of the capital investment multiplier table, CIMT (0.5), is reduced from the standard value (Fig. 1), population and pollution increases are substantially reduced, and natural resources remaining are substantially increased When the capital investment generation constant is varied from 0 040 to 0 060, maximum population and maximum pollution increase appreciably, the variables becoming oscillatory for the larger values of CIGN, and the natural resources remaining are substantially decreased. The result of decreasing the capital investment discard constant (Fig 3) CIDN is similar to that produced by increasing CIGN

This last result is especially interesting, because it states that increasing the capital investment generation constant has the same general effect as decreasing the capital investment discard constant. Why this happens in the model is clear from equation (4). Increasing CIGN or decreasing CIDN has the effect of increasing the capital investment increment Whether this behaviour corresponds to that in the real world is another question

In addition to the sensitivities shown in Figs 1–3, I examined the effect of varying one point in each of the two pollution Tables POLCMT (2 0) over the range 2 0 (0 5) 4 5 and POLATT (0) over the range of 0 1 (0.1) 0 7 By varying the one point in either one of these Tables, the maximum pollution was increased by a factor of 4 over the standard case

S-Shaped Growth

"Examples of growth systems," according to Kaysen, "are known that display quite different behaviour as they approach their natural limits than the sharp reversals portrayed in *Limits* For instance, a system in which the rate of growth of the major variables was proportional to their distance from their limit would show a smooth, gradual, stable adaptation to its growth ceiling" (ref 2, page 661). This comment was examined briefly with regard to population by introducing a

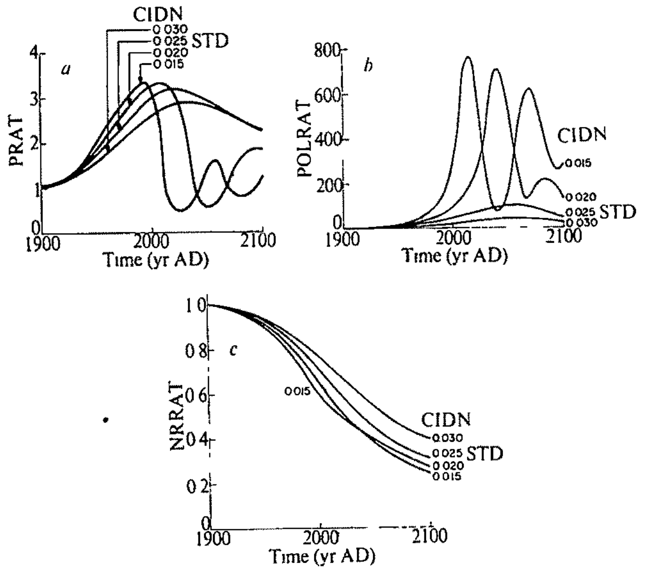

Fig 3 Effect of varying the capital investment discard normal (CIDN) Time variation of, *a*, normalized population (PRAT), *b*, normalized pollution (POLRAT), *c*, normalized natural resources remaining (NRRAT)

factor [1-$P(t)$/PMAX] into equation (1) Whereas that equation states population is determined by

$$P(t+\Delta t)=P(t)+\Delta t[\mathrm{BR}-\mathrm{DR}], \tag{1}$$

I modified this to

$$P(t+\Delta t)=P(t)+\Delta t[\mathrm{BR}-\mathrm{DR}]\ [1-P(t)/\mathrm{PMAX}], \tag{1a}$$

where the new factor was applied only for time greater than 1970 Before 1970, which may be regarded as the "awareness time", equation (1) was used The growth mode defined by equation (*1a*) is here called "S-shaped growth" Because this modification reduces the population increment more as the population approaches an assumed maximum, PMAX, it may simulate the fact that as people become more aware of a problem, in this case overpopulation, they will apply various kinds of constraints

In these runs, PMAX was varied from 1 5 to 5 0 times the 1900 population (PI) in increments of 0 5 The standard model corresponds to PMAX infinite Briefly, as PMAX/PI was increased from 1 5 to 5 0, the peak population (PRAT) increased by 30%, the peak pollution (POLRAT) decreased by 100%, the NRRAT remaining in 2100 increased by 0 3%, and the peak normalized capital investment decreased by 1 5% In other words, a substantial change in population was accompanied by a negligible change in capital investment and natural resources Another interesting result was the decrease in pollution as the population increased

Of course, the same technique to simulate S-shaped growth can be applied to the other state variables, and the "awareness times", 1970 in equation (*1a*), can be independent for each variable A possible way of applying the "awareness" concept to capital investment might be to allocate different fractions of capital investment to specific problems, for example, pollution or natural resources, with the fraction determined by how close the world has come to a preset limit

Conclusions on Parameter Variations

Clearly, the model is sensitive to the input assumptions, especially so with respect to those about capital investment and pollution It is also noteworthy that population is very sensitive to capital investment changes while capital investment is relatively insensitive to population Some of the variables show a pronounced tendency to oscillate, such as population in Figs 2*a* and 3*a* and pollution in Figs 2*b* and 3*b* These results concerning sensitivity point in one of three principal directions. either the World Dynamics Model is basically a correct description of the world, but requires a more accurate set of inputs (Tables and constants), or the world is indeed very sensitive to small changes, or the model has serious flaws and requires extensive re-examination As noted below, which direction is the more appropriate cannot be determined from within the simulation

Fundamental Considerations of the World Dynamics Model

I shall now discuss six considerations that are central to an understanding of the World Dynamics Model, and indeed to any attempt to simulate the world These go beyond the question of a particular Table or a particular constant

(1) The Axiom–Logic System The World Dynamics Model is a closed mathematical system with its own axioms and its own logical structure and must be examined as such. The Tables and constants constitute the axioms, and the equations constitute the logical structure The pollution crisis N yr later, for example, is built into the assumptions of the model even though this is not apparent because of the model's complexity There is a close parallel between this situation and that of Euclidean geometry where the Pythagorean theorem is built into the set of axioms and the logic There is no more convincing proof of this than the geometries of Riemann and Lobachevski, where, by changing one Euclidean axiom, these men produced completely different geometries The fact that we find Euclidean geometry useful in many practical applications is fortuitous, but the justifications for these applications certainly do not follow logically from Euclid's closed mathematical system In a similar sense, any relationship between the results of the World Dynamics simulation and the situation in the real world has to be established and argued outside the simulation The most one can hope for is that use of the model may inform and illuminate the search for an understanding of the world situation

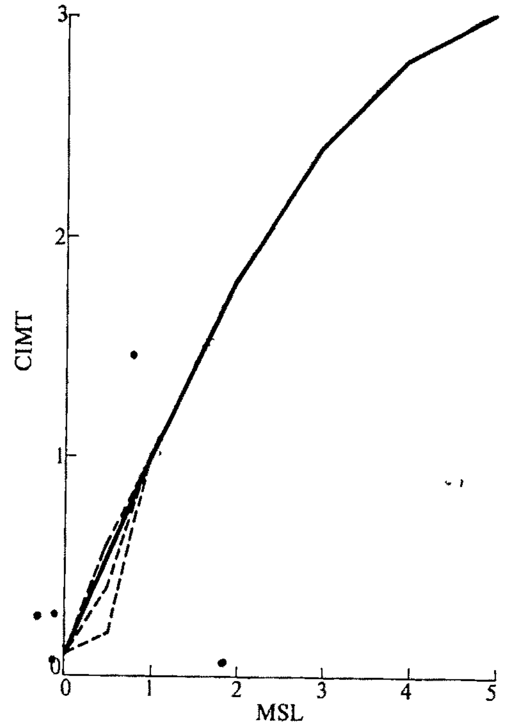

Fig. 4 Capital investment multiplier (CIMT) as a function of mean standard of living (MSL) - - -, Effect of changing the value of CIMT (0 5) All curves are identical for MSL greater than 1

(2) Spatial Homogeneity. Many commentators have noted that the level of aggregation in Forrester's simulation is too high, that describing the capital investment policy of the world—the Western world, the Socialist world, and the underdeveloped world—in one equation cannot lead to useful results. The results given above about the sensitivity of the capital investment equations give point to this concern. One could argue that a low capital investment multiplier for a low material standard of living is a reasonable description of an uncontrolled, underdeveloped economy, but a very poor description of a highly controlled economy. What multiplier would be appropriate for a developed, partially controlled economy is still another relevant question. Indeed, is a single capital investment multiplier Table a useful concept?

(3) Temporal Homogeneity. The World Dynamics simulation makes the fundamental assumption that a tabular relationship, at best determined with data available up to time *t*, is valid for all future time. Because these Tables must in some way include the integrated effects of many changes in transportation, energy, birth control, communications, social systems, to mention just a few, it is difficult to imagine that equally competent investigators would choose the same Table of values for each variable in 1900, 1971, or 2042. But the sensitivity analysis shows that these choices are critical to the outcome. The assumption that Tables can be valid for more than a century after the relevant data were collected asserts a greater understanding of human dynamics than most social scientists claim.

(4) Identification of State Variables. The identification of the state variables and the factors that will enter into their computation is as crucial in the World Dynamics simulation as in any simulation. Would a competent investigator in 1900 have identified pollution as a major variable for the next 200 yr? Is it possible that the amount and control of thermonuclear fuel will be the crucial variable 100 yr hence? Although the choice of state variables in the World Dynamics Model may seem reasonable today, one would probably want more support before committing the simulation to these five exclusively. It would be interesting to examine what factor analysis and other statistical methods can contribute to the choice of variables and their relative weights.

(5) Modes of Growth. A further consideration is that population in the World Dynamics Model is based on the difference equation of exponential growth

$$P(t+\Delta t)=P(t)+K[P(t)]\Delta t$$

where K is a function of time and other variables. As has already been suggested by Kaysen, there are other growth mechanisms, and I have illustrated at least one such. It would be interesting to learn what justification one could adduce for different growth mechanisms. In any case, the equations of growth are important to a simulation of the world, and they should bear a good deal of scrutiny in any model.

(6) Accuracy of Data. Finally, the World Dynamics Model admittedly is not based on detailed world data, so it may not be fair to criticize it because it happens to be sensitive to some input assumptions. But the analysis does suggest accuracy levels that should be met if one accepts the model. Additionally, if the accuracy requirements turn out to be great, one may be confronted with definitional problems. This is a frequent consequence of more precise measurements of more extensive data requirements.

I thank E. L. Kay and S. E. Rose for encouragement.

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Appendix

This appendix contains, in algebraic notation, a description of the World Dynamics Model program (ref. 1, pages 132–137). Whereas that program used 111 symbols or variable names, the following description does not contain so many because many of them are, in some sense, duplicates, some are control variables, and some are not used in the standard model.

In the following description, which contains the exact substance of the standard model, four notational elements are used. (a) A set of contiguous letters constitutes a variable name (for example, MSL is material standard of living, BR is birth rate and so on). (b) Brackets are used to indicate multiplication. (c) Variable names ending in "T" refer to Tables used in the model (such as CIMT, the capital-investment-multiplier Table). (d) Parentheses are used to indicate functional notation. Thus NRMMT (MSL) is the ordinate in the NRMMT Table corresponding to the independent variable MSL. The tables used by Forrester are defined in the program, graphs and justifications for the Tables are given in *World Dynamics* (ref. 1, chapter 3).

Set Initial Conditions

Time step of simulation, $\mathrm{DT}=0.2$ yr
Initial population, $\mathrm{PI}=1.65\times10^{8}$ people
Initial capital investment, $\mathrm{CII}=4\times10^{8}$ units
Initial pollution, $\mathrm{POLI}=2\times10^{8}$ units
Initial capital-investment-in-agriculture-fraction, $\mathrm{CIAFI}=0.2$
Initial natural resources, $\mathrm{NRI}=9\times10^{11}$ units
Time, $t=0$

Calculate the Independent Variables

$\mathrm{NRFR}=\mathrm{NR}(t)/\mathrm{NRI}$
$\mathrm{NREM}=\mathrm{NREMT(NRFR)}$
$\mathrm{CIR}=\mathrm{CI}(t)/P(t)$
$\mathrm{MSL}=\mathrm{CIR}[1\text{-}\mathrm{CIAF}(t)]\mathrm{NREM}/0.7$
$\mathrm{POLR}=\mathrm{POL}(t)/(3.6\times10^{9})$
$\mathrm{FPM}=\mathrm{FPMT(POLR)}$
$\mathrm{CR}=P(t)/(1.35\times10^{8}\times26.5)$
$\mathrm{FCM}=\mathrm{FCMT(CR)}$
$\mathrm{CIRA}-\mathrm{CIR}[\mathrm{CIAF}(t)]/0.3$
$\mathrm{FPCI}=\mathrm{FPCIT(CIRA)}$
$\mathrm{FR}=[\mathrm{FPCI}][\mathrm{FCM}][\mathrm{FPM}]$
$\mathrm{QLM/QLF}=\mathrm{QLMT(MSL)/QLFT(FR)}$

Calculate Population

$$\mathrm{BR}=0.04\ P(t)[\mathrm{BRCMT(CR)}][\mathrm{BRFMT(FR)}][\mathrm{BRMMT(MSL)}][\mathrm{BRPMT(POLR)}]$$

$$\mathrm{DR}=0.028\ P(t)[\mathrm{DRCMT(CR)}][\mathrm{DRFMT(FR)}][\mathrm{DRMMT(MSL)}][\mathrm{DRPMT(POLR)}]$$

$$P(t+\mathrm{DT})=P(t)+\mathrm{DT}[\mathrm{BR}-\mathrm{DR}] \tag{1}$$

Calculate Capital Investment

$\mathrm{CIGN}=0.05$

$\mathrm{CIDN}=0.025$

$$\mathrm{CIG}=[\mathrm{CIGN}][\mathrm{CIMT(MSL)}]P(t) \tag{2}$$

$$\mathrm{CID}=[\mathrm{CIDN}]\mathrm{CI}(t) \tag{3}$$

$$\mathrm{CI}(t+\mathrm{DT})=\mathrm{CI}(t)+\mathrm{DT}[\mathrm{CIG}-\mathrm{CID}] \tag{4}$$

Calculate Pollution

$$\mathrm{POLG}=[\mathrm{POLCMT(CIR)}]P(t) \tag{5}$$

$$\mathrm{POLA}=\mathrm{POL}(t)/[\mathrm{POLATT(POLR)}] \tag{6}$$

$$\mathrm{POL}(t+\mathrm{DT})=\mathrm{POL}(t)+\mathrm{DT}[\mathrm{POLG}-\mathrm{POLA}] \tag{7}$$

Calculate Capital-Investment-in-Agriculture-Fraction

$$\mathrm{CIAF}(t+\mathrm{DT}) = [1-\mathrm{DT}/15]\mathrm{CIAF}(t) + [\mathrm{DT}/15][\mathrm{CFIFRT}(\mathrm{FR})][\mathrm{CIQRT}(\mathrm{QLM}/\mathrm{QLF})] \tag{8}$$

Calculate Natural Resources

$$\mathrm{NR}(t+\mathrm{DT}) = \mathrm{NR}(t) - \mathrm{DT}[\mathrm{NRMMT}(\mathrm{MSL})]P(t) \tag{9}$$

Calculate Quality of Life

$$\mathrm{QL}(t) = [\mathrm{QLMT}(\mathrm{MSL})][\mathrm{QLCT}(\mathrm{CR})][\mathrm{QLFT}(\mathrm{FR})][\mathrm{QLPT}(\mathrm{POLR})] \tag{10}$$

Increment time by DT

Go to "Calculate the Independent Variables"

When simulation is complete, print and plot results

Definition of Symbols

BR	Birth rate (people yr^{-1})
BRCMT	Birth rate from crowding multiplier Table
BRFMT	Birth rate from food multiplier Table
BRMMT	Birth rate from material multiplier Table
BRPMT	Birth rate from pollution multiplier Table
CFIFRT	Capital fraction indicated by food ratio Table
CI	Capital investment (capital units)
CIAF	Capital investment in agriculture fraction (dimensionless)
CIAFI	Capital investment in agriculture fraction, initial (dimensionless)
CID	Capital investment discard (capital units yr^{-1})
CIDN	Capital investment discard normal (fraction yr^{-1})
CIG	Capital investment generation (capital units yr^{-1})
CIGN	Capital investment generation normal (capital units per person yr^{-1})
CII	Capital investment, initial (capital units)
CIMT	Capital investment multiplier Table
CIQRT	Capital investment from quality ratio Table
CIR	Capital investment ratio (capital units per person)
CIRA	Capital investment ratio in agriculture (capital units per person)
CR	Crowding ratio (dimensionless)
DR	Death rate (people yr^{-1})
DRCMT	Death rate from crowding multiplier Table
DRFMT	Death rate from food multiplier Table
DRMMT	Death rate from material multiplier Table
DRPMT	Death rate from pollution multiplier Table
FCM	Food from crowding multiplier (dimensionless)
FCMT	Food from crowding multiplier Table
FPCI	Food potential from capital investment (food units per person yr^{-1})
FPCIT	Food potential from capital investment Table
FPM	Food from pollution multiplier (dimensionless)
FPMT	Food from pollution multiplier Table
FR	Food ratio (dimensionless)
MSL	Material standard of living (dimensionless)
NR	Natural resources (natural resource units)
NREM	Natural resource extraction multiplier (dimensionless)
NREMT	Natural resource extraction multiplier Table
NRFR	Natural resource fraction remaining (dimensionless)
NRI	Natural resources, initial (natural resource units)
NRMMT	Natural resource from material multiplier Table
P	Population (people)
PI	Population, initial (people)
POL	Pollution (pollution units)
POLA	Pollution absorption (pollution units yr^{-1})
POLATT	Pollution absorption time Table
POLCMT	Pollution from capital multiplier Table
POLG	Pollution generation (pollution units yr^{-1})
POLI	Pollution, initial (pollution units)
POLR	Pollution ratio (dimensionless)
QL	Quality of life (satisfaction units)
QLCT	Quality of life from crowding Table
QLF	Quality of life from food (dimensionless)
QLFT	Quality of life from food Table
QLM	Quality of life from material (dimensionless)
QLMT	Quality of life from material Table
QLPT	Quality of life from pollution Table
TIME	Calendar time (yr)

Positional Information in Chick Limb Morphogenesis

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Pattern formation by the cells of a growing organism depends on coordination of changes in space and time. Evidence is presented here for the control of morphogenesis by positional information specified by an autonomous timing mechanism that operates in a "progress zone" at the tip of the limb bud.

SPATIAL patterns of cellular differentiation may be established by a two step process the cells may first have their positions specified with respect to certain boundary or reference regions, as in a coordinate frame, and may then interpret this positional information by selecting an appropriate course of differentiation, according to their genome and developmental history[1,2] The idea of positional information has so far been applied principally to regulative systems such as insect epidermis[3] and *Hydra*[4], where growth is not a prominent feature For these systems some quite successful models have been developed, involving two gradients, one in a diffusible substance, acting as a signal of position, and another in a more stable cell parameter which may be considered as an intrinsic positional value. The diffusible signal gradient may be maintained, for example, by a source at one boundary and a sink at another[5]. The models embody rules for the interaction between the two gradients

Here we show how positional information may be assigned and used to pattern a growing organ, the embryonic chick limb The mechanism is different from those mentioned above, according to which cells read positional information from the local value of a position-dependent signal. Just as navigation can depend on clocks as well as maps, so the intrinsic positional character of cells and tissues may be decided by a combination of spatial and temporal cues. In particular, specification by timing can supplant specification by a graded signal maintained by localized sources and sinks. This is especially true for patterns laid down in the course of growth.

For example, as the limb grows out and lengthens, the more and more distal positional values may be allocated just behind its advancing tip at later and later times. The tissue at the very tip can, through growth, serve as a source of the new distal territories, while its own positional character remains in a state of flux. The tissue that emerges early from the labile tip region, in this type of outgrowth, will be proximal; the tissue that emerges late will be distal. The positional character of a group of cells may therefore be decided by the length of time that they or their ancestors have spent in the labile tip region. Some spatial signal is needed to mark out the extent of that region, but this is the only cue that the surrounding tissues must supply to generate the proper proximo-distal sequence of parts. There is no need for an external signal to specify positional value. The specification may, instead, depend entirely on the timing of the stay in the labile region, if there, and only there, tissue changes spontaneously to become steadily more distal in its intrinsic character.

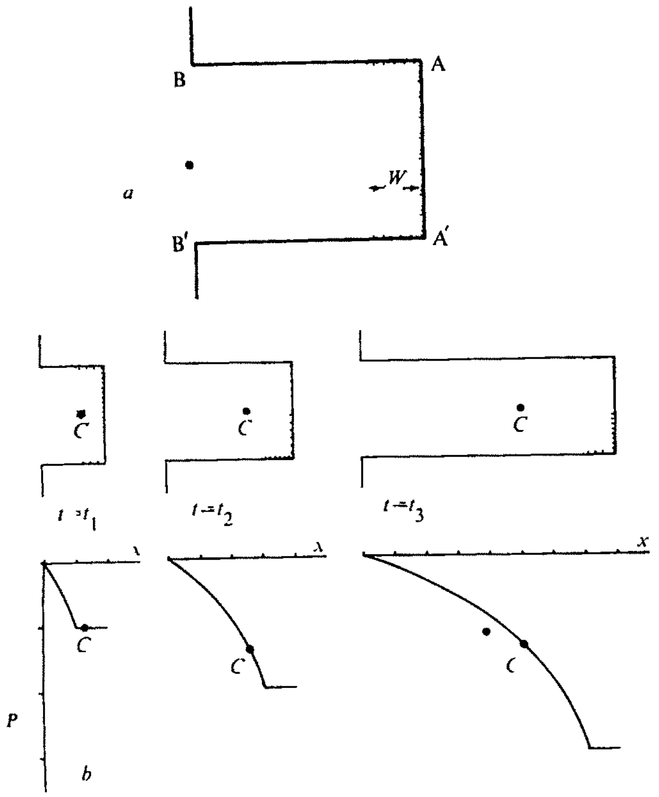

Fig. 1 *a*, An idealized outgrowth. BB′ is its base, and AA′ is its tip. The progress zone, of width *W*, is marked by shading. *b*, The positional value *P* is shown as a function of the distance *x* from the base of the idealized outgrowth at three successive times, t_1, t_2, t_3. *C* marks the mean position of one typical cell lineage followed through the three ages. Inside the progress zone, *P* is taken to change at a rate proportional to the rate of cell proliferation, while elsewhere *P* is fixed so that the pattern of positional values can only spread out by interstitial growth. Note that the size of the progress zone governs the size of the structures that emerge. If the zone were reduced to half its normal width, the full normal range of positional values would initially be crammed into only half the normal expanse of tissue: each anatomical rudiment would be only half its normal length.

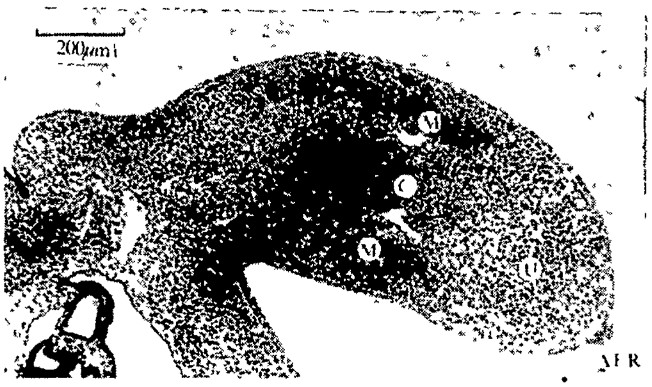

Fig. 2 A stage 23 chick wing bud sectioned in the plane of the proximo-distal and dorso-ventral axes. (Fixed in Karnovsky's fixative, embedded in 'Araldite', cut at 1 µm, and stained with toluidine blue.) AER, apical ectodermal ridge, U, undifferentiated tip mesenchyme, M, pre-muscle, C, pre-cartilage.

If the rate of this spontaneous change is proportional to the rate of cell division in the labile region, then the assignment of positional values will always be harmoniously linked with growth; the pattern will be tailored to the size of the system at every stage. This is an important consideration for almost all embryos, both plant and animal, whose growth may often be hastened or delayed by chance variations of temperature. There is some direct evidence that cells in a different type of system, an insect epidermis[3], can change their intrinsic positional value only when they divide. In the type of outgrowth described here, cell division may continue outside the labile region, but there it will not be associated with a change of positional value. A labile region where new positional values are successively engendered in the course of growth, we shall call a "progress zone". For an idealized system (Fig. 1*a*) growing out uniformly along one axis with a progress zone at its tip, we obtain, at successive times, the patterns of positional value shown schematically in Fig. 1*b*.

We shall now argue that the embryonic chick limb does in fact develop by such a mechanism. We shall consider only the proximo-distal organization. There is substantial evidence that the antero-posterior coordinate of positional value is specified in a different way, involving some kind of signalling from a polarizing region close to the posterior border of the limb bud[1,6]; very little is known about the dorso-ventral axis.

The Chick Wing

The chick wing bud starts as a very small bulge from the flank, and grows out as a tongue-shaped mass, consisting of mesenchyme encased in ectoderm. The ectoderm is even and featureless, except for the apical ectodermal ridge, a thickening running round the distal rim of the bud. Earlier work has emphasized the interactions between the mesenchyme and this ectodermal ridge in relation to limb outgrowth[6–8]. We have suggested that the overall shape of the limb bud may depend on the mechanics of the ectoderm and in particular on the strengthening role of the apical ridge[9].

We wish here to focus attention on the mechanism by which the skeletal elements along the proximo-distal axis are specified, each with its own distinctive character. These are laid down within the mesenchyme in a proximo-distal sequence[10]: the primordia of proximal structures begin to differentiate first, while the primordia of more distal structures appear at successively later times and more distal positions. But the tip, that is, the layer of mesenchyme extending inwards from the apical ridge for about 400 µm, remains apparently undifferentiated up to stage 28 or so (Fig. 2), and continues to proliferate relatively rapidly[11]. We find autoradiographically that all the cells there are

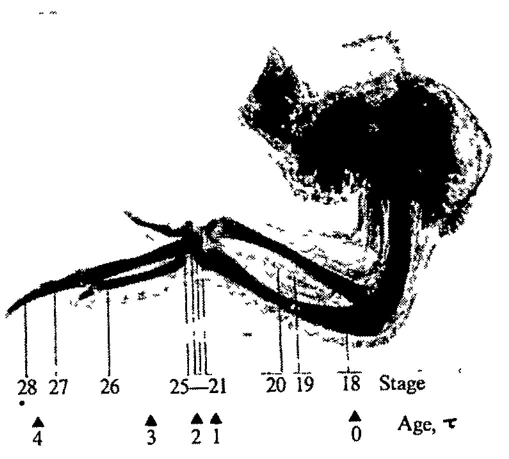

Fig 3 The mean level of truncation is shown following apical ridge excision at each of the stages indicated The mean for each stage is derived from measurements of at least seven cases Beneath the stage numbers we mark the estimated age τ defined as the number of cell divisions that have elapsed in the tip mesenchyme since stage 18, when the limb bud first begins to bulge out Note the bunching of results at the wrist This is due to a relatively high cell density and low proliferation rate in that region after it emerges from the apical zone (D S and J H L, unpublished) The truncated limbs and contralateral controls were fixed in 5% TCA at 9–10 d incubation, stained with alcian green, and cleared in methyl salicylate for measurement

actively dividing, the distal cells have been reported also to preserve a "morphogenetic potential" at stages when proximal cells have already lost it[12] We suggest that there is a progress zone located within this mesenchyme beneath the apical ridge, that is, the tip of the limb bud is a region of change, generating tissue with new and progressively more distal positional values These positional values are interpreted by the cells to give the sequence of distinctive structures

Removal of the Apical Ridge

A classical experiment of Saunders[10] shows that the lability of the tip mesenchyme depends on the presence of the apical ectodermal ridge Saunders found that if the apical ectodermal ridge is cut off, the limb fails to develop distal elements it is normal up to a certain level beyond which there is nothing The later the stage at which the ridge is removed, the more nearly complete the resulting limb Conversely, when a supernumerary ridge is grafted onto the dorsal surface of a limb bud, a secondary distal axis develops beneath it[6] We have repeated and extended (D S and J H L, unpublished) Saunders's series of experiments of the former type with a view to providing more quantitative data, and have measured the lengths of the various skeletal elements, using the undisturbed side as control[13]

In Fig 3 we show the cut-off level following apical ridge removal between stages 18 and 28 In the terms of our theory, apical ridge removal halts the change of positional value in the apical mesenchyme when the ridge is removed progress stops in the zone at the tip The cells there lose their lability prematurely, reduce their rate of proliferation, and start to differentiate according to their current positional value The resulting limb is therefore shorter, lacking not only the most distal positional values, but also the cells which would have expressed them

By excising the apical ridge, we assay for the positional value at the tip If, for example, we halt all changes of positional value at stage 22, and obtain a limb truncated at the wrist, the most distal positional value in the stage 22 limb bud must have been that corresponding to the wrist The assay is, however, marred by two uncertainties, we do not know accurately the extent of trauma, nor how promptly the positional value stops changing after the apical ridge is removed Disregarding this correction, we can now reinterpret Fig 3, it shows, for each stage, S, from 18 to 28, which eventual limb structure has the same positional value as stage S tip tissue We can use it in conjunction with presumptive fate maps to deduce the width of the progress zone Our analysis gives 300±100 μm as a rough estimate (D S and J H L, unpublished)

Grafting of Distal Tips

There is evidence that the course of the change in proximodistal positional value which occurs in the progress zone is governed by its internal autonomous kinetics rather than by a level-specific signal from outside, for example from the apical ectoderm or the stump The elegant and crucial work of Rubin and Saunders[14] has shown that the influence of the apical ridge does not determine the axial level of the underlying mesenchyme They showed that ectodermal caps can be exchanged between limb buds of different ages, each then developing into a normal limb In terms of our model, the apical ectodermal ridge is needed to keep the mesenchyme labile at the tip, but it does not direct the path of progress there The ridge issues a general permit rather than specific instructions

From experiments in which the tips of two limb buds of different ages are exchanged (Fig 4*a*) specification within the progress zone by a signal from the proximal stump can be ruled out If both pieces of each composite bud develop according to their original presumptive fates, some parts of the resulting limbs will be missing or duplicated If the stumps signal positional values to the tips, however, the presumptive fates of the tips will be radically modified Our results, which will be reported in detail elsewhere, show that at least when the grafted tip is more than about 300 μm wide (that is, 300 μm from cut surface to apical ridge), the presumptive fate of the tip is not altered except perhaps in the immediate vicinity of the junction Deficiencies and reduplications are regularly produced, and the measured size and form of the grafted distal regions resemble those of the donor control limb (Figs 4*a–c* and 5) These findings clearly exclude long-range signals controlling either growth or pattern formation in the distal region, and in particular rule out humoral mechanisms and mechanisms whereby elements already formed inhibit formation of further similar elements[15] Similar results have been recorded by Amprino *et al*[16], but Hampé[17] and Kieny[18,19] have emphasized the regulative capacity of the chick limb bud, and have reported that grafted distal tissue may sometimes be converted to a more proximal character by the influence of proximal host tissue Their evidence, however, is not compelling, and is not corroborated by further experiments of our own (D S and J H L, unpublished) The regulation they observe occurs chiefly in grafts of apical slivers so thin that the progress zone due to the apical ridge of the graft can extend into the host, and there bring about considerable regeneration of excised parts without any signalling of positional value We do not rule out the possibility of some short-range interaction, however, by which cells cooperate to adopt a locally uniform, compromise character Such a local smoothing interaction may well occur at the time of differentiation, outside the progress zone, and over short distances affect the histological interpretation of positional value It could also occur earlier, inside the progress zone, and directly affect the assignment of positional value We do not know how far the autonomy seen on a coarse scale corresponds to autonomy of individual cells

Application to Other Systems

The idea that positional information might be specified in growing fields by a timing mechanism, such as the counting of cell divisions in a labile zone, seems applicable to a variety of other systems It could, for example, explain how positional values are assigned within a blastema so as to follow the rule of distal transformation[2]. If blastema formation involves setting up a progress zone from the cells at the cut surface, then the regenerate will automatically originate at the positional value corresponding to the level of the cut, and from there develop only the more distal levels. Thus, for example, a blastema on the proximal face of the distal half of an amputated structure will yield a mirror image regenerate. This phenomenon occurs in the regeneration of both amphibian limbs[20] and insect imaginal disks[21]. A timing mechanism may also specify positional values in the retina, where they may be used for making the regular pattern of retino-tectal connexions[22]. Up to the stage when the system has its polarity specified, there is uniform cell division[23], but after this, growth is confined to a relatively narrow ring near the outer edge[24]. Thus cells at the outer edge of the mature retina have divided more times than those nearer the centre. There may thus be a progress zone during retinal growth which could provide the retinal cells with a radial coordinate analogous to the proximo-distal coordinate in the limb.

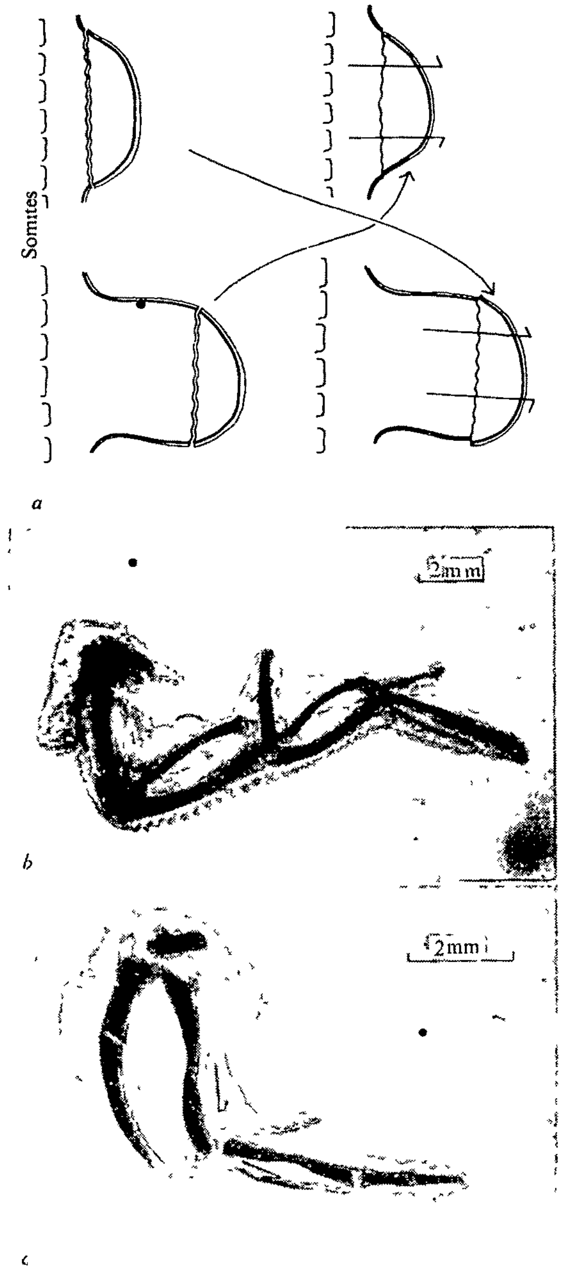

Fig. 4 *a–c*, The whole of a stage 19 wing bud is exchanged with the distal quarter of a stage 24 wing bud (*a*, dorsal view). The grafts are held in place with pins. The outcome corresponds with negligible regulation. Typically a young bud on an old stump (*b*) gives a humerus and forearm of the same length as in the host's contralateral control wing, followed by a humerus, forearm and hand of the same length as in the donor's control wing. By contrast, an old tip on a young stump (*c*) gives a humerus of the same size as in the host's control wing, followed by a hand of the same size as in the donor's control wing. (The photographs in fact show composite limbs from two different pairs of chicks.)

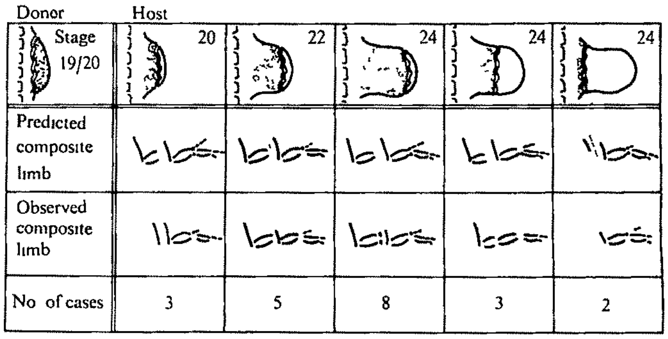

Fig. 5 An entire young wing bud is grafted on an older host stump, as in Fig. 4*a*. The stages of donor and host are as marked on the sketches in the top line. The predicted outcome is derived from fate maps[28] assuming no interaction between host and donor. The observed outcome is a mean, derived from measurements on several composite limbs, the number of measured limbs is shown in the bottom line. Apart from some possible local regulation affecting not more than about half an element, the observations agree with the predictions.

Specification of Positional Value

We have proposed a new mechanism, based on autonomous changes of positional value with time rather than on signals from far off, to specify positional information in a growing system. On this basis, a model can be developed to give quantitative predictions of the outcome of various grafts, and these predictions are consistent with the experimental data (D. S. and J. H. L., unpublished). Several questions now require further investigation. For example, how is positional value registered by individual cells and is it a continuous variable? Does it change only at cell division, suggesting an analogy with regulation in the insect epidermis[3] and with Holtzer's "quantal mitosis"[25]? Are individual cells autonomous, or is there local averaging of positional value by short-range communication between cells inside or outside the progress zone? How does the apical ectodermal ridge specify the width of the progress zone, is hyaluronic acid involved, as some recent experiments[26] perhaps suggest?

More generally one can begin to see how positional information may be specified in different systems, using, in different ways, three principal components: a positional value, a positional signal, and cell division. In *Hydra* a new boundary region may be formed when the signal is a threshold amount below the positional value, in the insect epidermis the positional signal sets the positional value at cell division, in the vertebrate limb bud the positional value changes autonomously at cell division, and in intercalary regeneration in the insect limb differences between the signal and the intrinsic value may initiate cell division[27]. Our analysis of the chick limb strongly indicates that one should look for a biochemical correlate to the proposed changes in positional value in the porgress zone. While suggesting where to look, and what to look for, it unfortunately provides no indication whatsoever as to how to do it.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Distance Measurements across the Heimaey Eruptive Fissure

In describing the latest Icelandic eruption, Kirkjufell, Thórarinsson *et al.*[1] showed how it began as an erupting fissure about 1,500 m long and how activity ceased on all but the central three vents after 3 d. We have made precise distance measurements between four fixed stations located around the southern end of the fissure (Fig. 1) on two visits in February and April. The measurements, made with the National Physical Laboratory Mekometer III prototype[2,3], corrected for atmospheric refractive index and modulating frequency, are shown plotted with their expected errors against time in days after January 23 on Fig. 3. Also shown on Fig. 3 are the curves of the form

$$d=d_0(1-\exp(aT))$$

where d is the strain at time T, d_0 is the strain at time zero and a is the inverse of a time constant, which best fit the observed results. Each best fit has the same time constant, 7.5 d, and is in good agreement with the observations, excepting the April result of line 3–1A.

We have thus assumed that the observed strains result from a single system which relaxed exponentially after the start of the eruption with a time constant of 7.5 d. The relaxation continued in this way for the two lines perpendicular to the fissure at least until early April, although some other process governed the changes on the longitudinal line, 3–1A, after February.

We calculated the asymptotes and lengths at time zero, and thus the recoverable strain at the time the eruption started, for each line. There is presumably also a non-recoverable component of unknown magnitude associated with the crustal spreading, so that our strain values must be minima. They are on line 1–2, 340 p.p.m., on line 3–4, −74 p.p.m., on line 3–1A, −409 p.p.m.

Ramsay[4] shows that the strain E in a direction θ to an orthogonal set of an extension E_1 and a compression E_2 is given by

$$E=\tfrac{1}{2}(E_1+E_2)+\tfrac{1}{2}(E_1-E_2)\cos 2\theta$$

Using our calculated values of the original strains on the three lines, we found that $E_1=36$ p.p.m. and $E_2=-420$ p.p.m., and that the axis of maximum compression is orientated at N 45° 21′ E. This is very nearly a state of pure shear, indeed the deviation of this result from pure shear may represent the crustal displacement produced by the eruption.

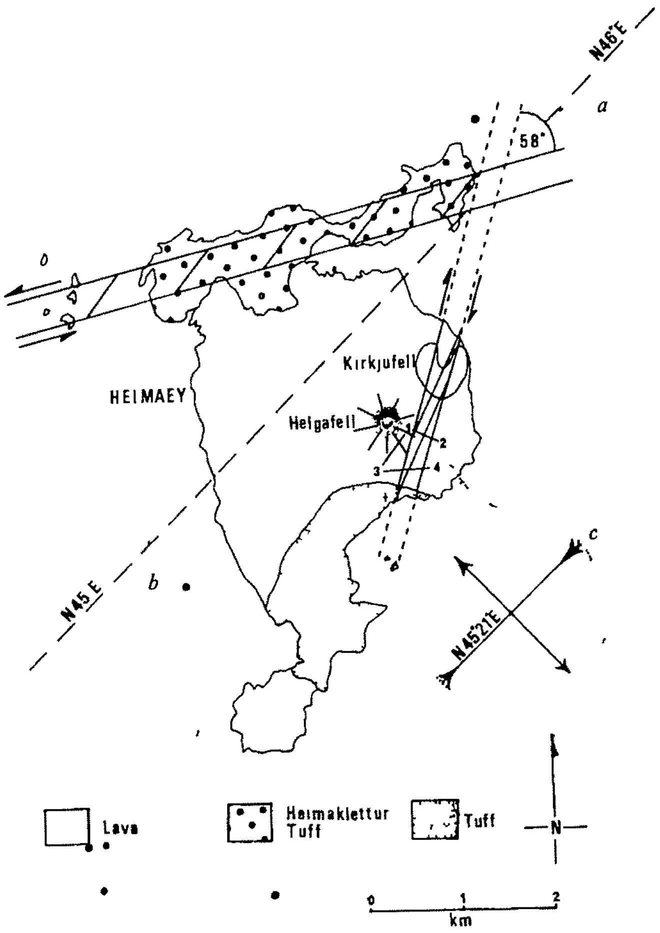

Fig. 1 Geological map of Heimaey showing the relationship between the distance measurements and the inferred shear zones. *a*, Direction of maximum compression to produce conjugate shear zones; *b*, regional trend of the active zone in south-central Iceland; *c*, maximum compression (Mekometer results). 1–2, Mekometer line.

Most observers[1] of the early activity along the whole length of the fissure consider that the active vents were in a straight line trending N 17° E, but our mapping by compass indicates that there are at least two sections of the fissure arranged *en echelon* The eight most southerly vents line up along N 24° E, and the line of the three vents still active in February has a N 27° E trend, this suggests a zone of right-lateral shear

Jakobsson[5] regards the Heimaklettur formation, the oldest on the island, as a fissure eruption, possibly subglacial, trending N 75° E, but composed of five *en echelon* units whose individual strikes are about N 35° E, this suggests a zone of left-lateral shear, the strike of which differs from that of the present eruption by 58° (Fig 1)

Similarly, Thórarinsson[6] described the submarine activity during the Surtsey eruption as being on a system of fissures with trends of about N 35° E covering a zone 5 km long and striking at N 65° E, as in the case of Heimaklettur, this suggests a zone of left-lateral shear

Assuming these three inferred shear planes to belong to the same conjugate set, the axis of maximum compression should lie in the plane bisecting the angle between the left and right-lateral members, N 46° E (Fig 1), almost the same as both the compressive direction deduced from the original strains calculated from the Mekometer results and the direction of the volcanic and tectonic features in the south-central active zone in Iceland

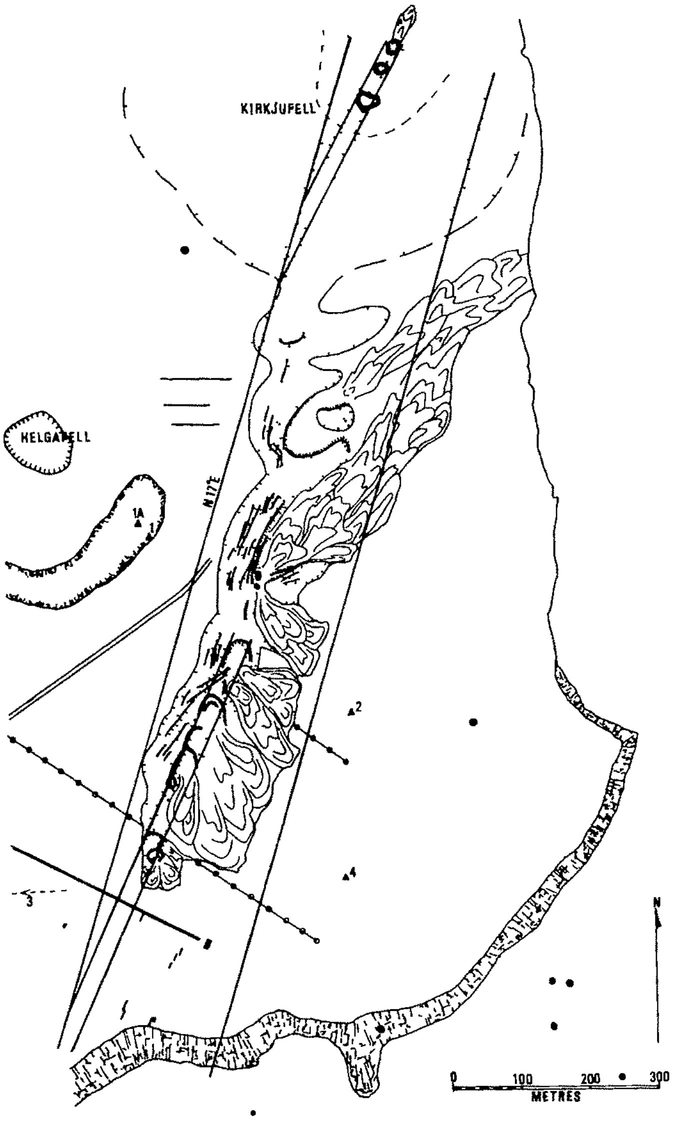

Fig. 2 Geological map of the southern part of the active fissure (February 7) ▲, Mekometer station, /, fissure

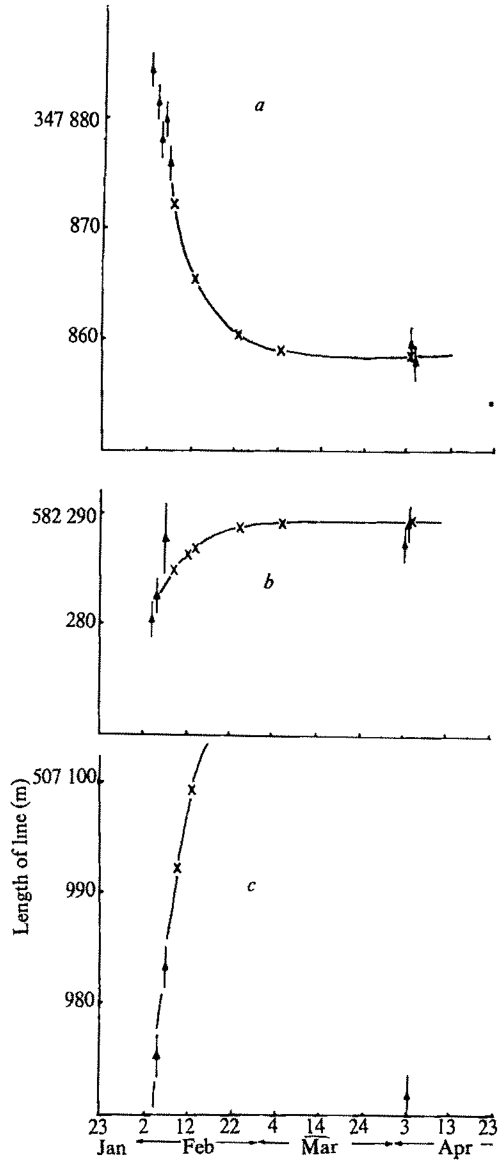

Fig. 3 Changes in length of the three measured lines from February to April ▲, Mekometer measurement with standard deviation, ×, theoretical exponential relaxation of strain *a*, Line 1–2, *b*, line 3–4, *c*, line 3–1A

There are two important conclusions to be drawn from these results First, they show that not all eruptions show the radially symmetric strain pattern of detumescence proposed by Mogi[7] and found in the eruptions of Kilauea[8] The difference presumably lies in the linearity of this eruption, and it might even be that all linear eruptions result from applied shear stresses Second, the inferred stress system agrees very well with the proposed spreading axis through the south-central active zone in Iceland, as it shows a minimum compression acting at N 44° W, almost exactly the expected spreading direction Heimaey lies at the extreme southern end of this zone, which may explain why the normal faulting associated, from seismological evidence[9], with spreading ridges, and indeed found further north, has given way to the observed shear tectonics

We consider that such a change in the tectonic response along the axis could come about through a relative southward decrease of the least compressive stress The petrochemistry of the basalts from this spreading axis shows a gradual change southward also, with tholeiites predominant further north, transitional basalts in the Hekla-Katla region and alkali-olivine basalts in the Vestmannaeyjar[10]

This decrease of the least compression towards the end of the spreading axis we consider to lend support to Piper's model[11] and that it is therefore unnecessary to invoke a transform fracture zone in Southern Iceland in order to connect the Mid-Atlantic Ridge to the south-central active zone.

We thank Dr G. P. L. Walker for suggestions, the Icelandic authorities, especially Professors Thórbjorn Sigurgeirsson and Sigurthur Thórarinsson, for help, Dr K. D. Froome, Mr R. H. Bradsell and the Director of the National Physical Laboratory for making the prototype Mekometer available, and the Royal Society for financial support.

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Earth Tidal Amplitude and Phase

DURING the summer and autumn of 1970 a NASA Goddard Space Flight Center laser tracking system tracked the Beacon Explorer C spacecraft from the Goddard Optical Facility in Greenbelt, Maryland. The tracking system provided distance measurements to the satellite at a rate of one per second with a precision of 30 to 50 cm on as many as four consecutive passes each day, weather permitting. The satellite, Beacon Explorer C, carries laser retro-reflectors and is in a near circular orbit at an altitude of about 1,000 km with an inclination to the equator of 41°.

The laser range measurements to the satellite from this single tracking station have been used to determine its orbit for nearly five months in 1970 and, because the latitude of the tracking station is similar to the orbital inclination, the inclination is the best determined parameter. It is the inclination that we discuss here. The original purpose of this investigation was to try and observe the change in latitude of the tracking station arising from polar motion[1] but in the course of the analysis the perturbation of the inclination by the Earth and ocean tides had to be accounted for.

From a point in space, the basic tidal response of the Earth to the gravitational attraction of the Moon appears as a small elongation of the Earth's shape (bulge) in the general Earth-Moon line. A similar elongation, or distortion, is caused by and directed roughly towards the Sun. To an observer on a satellite, the tides appear as a distortion of the gravitational field arising from the tidal bulge which is associated with the motions of the Sun and Moon rather than the rotation of the Earth. Thus, the perturbations of a satellite orbit arising from the tides are primarily determined by the motion of the satellite and its orbit with respect to the Moon and Sun rather than with the motion of the Earth. Hence, to a satellite there are no significant perturbations associated with the large semi-diurnal and diurnal tides that are observed on the Earth but only with the tidal (and other) terms of longer period, such as a few weeks to years. For the Beacon Explorer C satellite the largest terms in the perturbation of the inclination have periods of 85 d, one coming from the Sun and the other from the Moon, and amount to the time required for the orbital plane of BE-C to rotate once (about 4.25° d^{-1}) with respect to the First Point of Aries and the node of the Moon's orbit. The other major terms have periods of 34 d and 10 d, corresponding to half the rotation period of the orbital plane with respect to the Sun and Moon respectively.

For a solid Earth the magnitude of the tidal perturbations of the orbit would be directly proportional to the magnitude of the physical distortion of the surface by the tides, representable in magnitude by Love's number k, which is the ratio of the tidal potential to the tide rising potential. But for the real Earth, the magnitudes of the perturbing forces are probably modified by the additional influences of the oceans and the true nature of these forces as they affect a satellite are not presently fully understood.

The orbital inclination of Beacon Explorer C has been determined on twenty-eight occasions in a period of nearly five months. Only laser range measurements from the Goddard tracking station were used in the analysis and each determination of the orbital inclination was obtained from data collected on four consecutive passes of the satellite, spanning a period of 6 h. The values of the inclination over the five month period showed considerable variation (about 20 arc s), as we expected, but after subtracting the perturbations caused by the Earth's gravity field, the Sun and Moon's gravity and solar radiation pressure, and allowing for the change in latitude of the station arising from polar motion, a variation of 2 arc s still remained. This remaining variation had a very distinctive structure which can be almost entirely explained as Earth tidal perturbations.

We have calculated the effect of the Earth tides on the orbit numerically from the simplest of tide potential models, that is, a second degree spherical harmonic expansion about an axis offset slightly from the direction of the tide rising body to allow for a phase lag in the tidal response of the Earth. In this representation no differentiation has been made between the continental crust and the oceans. The effect of both the solar and lunar Earth tides has been included in the orbital computations with the restriction that the Love number, k_2, and the phase, φ_2, are the same for both the lunar and solar tides.

The theoretical perturbation has been compared with the observed inclination residuals for several values of k_2 and φ_2. The initial comparisons were made with $\varphi_2=0$ from which it soon became apparent that k_2 was around 0.25. Prior to this analysis we had anticipated that k_2 would be in the range 0.29 to 0.31 because these are the values that are being obtained from surface measurements, such as horizontal pendulums[2] and seismicity[3]. For all values of k_2 near 0.25 the differences between the observed and computed values of the inclination showed systematic variation and it became necessary to introduce a phase lag (φ_2) into the perturbations. After several tests the values of

$$k_2=0.245\pm0.005 \text{ and } \varphi_2=3.2\pm0.5°$$

were obtained as the best values where the fit to the data was 0.045 arc s standard deviation. The essential effect of introducing the phase was to reduce the standard deviation of fit to the data by about 35%. Neglecting the phase altogether led to the same optimum value of k_2 but with a larger standard error. In Fig. 1 we show the residuals to the inclination (after all but the Earth tides have been removed) and the theoretical tidal perturbation for the optimum values of k_2 and φ_2. The agreement between the laser data and theory is evident.

The gravitational field model used in this analysis was GEM 1 (ref. 4) with modified values for the 19th degree and the 13th order terms with which the BE-C satellite is resonant. GEM 1 is a field complete to degree and order 12 with selected higher resonance terms and zonals out to degree 21. When the original GEM 1 (19,13) resonant terms were used in this analysis the residuals about the tidal curve showed a periodic structure of 0.063 arc s and period 5.5 d. This pattern was used to derive new values of the 19th degree and 13th order terms and the data were then reanalysed. The adjustment to the (19,13) terms amounted to approximately 15% in the cosine term and 20% in the sine term. It is with the GEM 1 gravity field containing these two modified coefficients that the present results have been obtained.

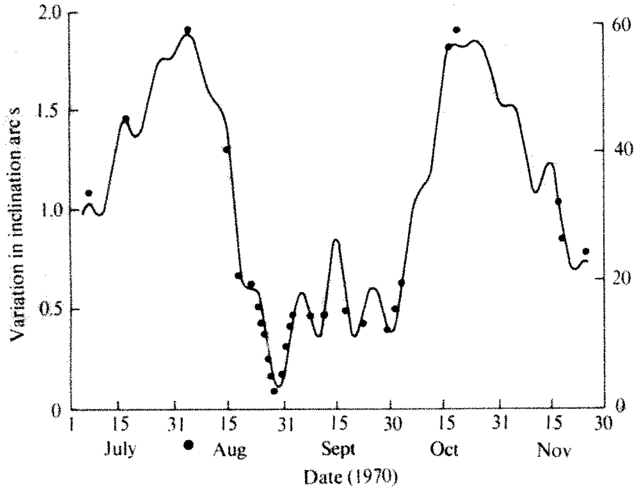

Fig. 1 The perturbation of the orbital inclination of the Beacon Explorer C spacecraft arising from the Earth and ocean tides. The dots are values of the orbital inclination derived from laser range measurements. The continuous line shows the theoretical perturbation computed from a second degree spherical harmonic representation of the solar and lunar tides with Love's number k_2=0.245 and a phase lag of 3.2°. The right hand vertical axis shows the variation in inclination projected onto the Earth's surface. The r.m.s. deviation of the observed points to the theoretical curve is 0.045 arc s (1.38 m).

The amplitude of the observed perturbation of the orbit is smaller than expected if the true value of Love's number, k_2, for the Earth is around 0.3, as is generally accepted. The simple model of the Earth tides upon which the theoretical curve was based must thus be inadequate. But the detailed agreement between the observed points and the theory necessitates the form of the perturbation for the BE-C satellite to be a second degree spherical harmonic. Thus, the perturbing influence that is modifying the computed tidal variation can only have a cancelling effect and in no way modify the form of the disturbing function for the satellite. W. H. Munk (personal communication) has indicated that this effect can probably be attributed to the ocean tides, and recent work by Lambeck and Cazenave[5] corroborates this view. Lambeck and Cazenave suggest that certain terms in the tidal potential function of the oceans cause perturbations of the orbit almost identical in form to the solid Earth tide. But the magnitudes of these ocean perturbations have a different variation with orbital parameters than the solid Earth perturbations. Thus, they suggest the observed tidal perturbations will depend on the orbit of the satellite being studied, and the determinations of k_2 (from satellites) so far[6-8] strongly support this viewpoint. Thus, orbital perturbation techniques may soon be in a position to provide quantitative information on certain components of the ocean tides.

The analysis reported here is probably the most precise determination to date of the amplitude and phase lag of the Earth and ocean tides from the tidal perturbations of a satellite. The use of high precision laser range measurements (30 to 50 cm) at a high repetition rate (1 s^{-1}) permitted the computation of very short orbital arcs of 6 h duration. This short averaging time permitted some of the fine structure of the perturbation to be revealed. The good agreement between observation and theory clearly shows that the tidal disturbing potential (for the Beacon Explorer C satellite) can be almost entirely represented by two second degree spherical harmonics offset by a few degrees from the directions of the Sun and Moon.

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Mesozoic Palaeomagnetic Scale of the USSR

WORLD data on palaeomagnetic Mesozoic stratigraphy have been summarized by several people[1-3]. The integrated palaeomagnetic reversal columns they obtained differ from one another partly because they have been drawn up from different data and partly because of small differences in the criteria used to define the fundamental palaeomagnetic stratigraphical units—palaeomagnetic zones. Here we give regional palaeomagnetic columns (Fig. 1) obtained recently as a result of detailed palaeomagnetic investigations of Mesozoic sedimentary formations of the USSR.

In order to coordinate the palaeostratigraphical data we used available USSR palaeomagnetic data[2-16] and the 1964 geochronological scale[17] of the USSR. Some errors caused by a lack of correlation between local stratigraphical scales and the integrated geochronological scale, the latter not being perfect itself, are inevitable. If radiometric determination of a stage boundary age has not been made and if only data concerning the boundaries between sections or systems are available, the time interval is divided into equal parts within the stage quantity (such boundaries are shown as diagonal lines in Fig. 1). At some parts of the section we assumed constant deposition rates ; thus we managed to translate from sections and beds to the time scale. This made it possible to estimate roughly the duration of palaeomagnetic zones. The geological time scale was divided in palaeomagnetic intervals and zones. These intervals and reversed (R) zones have been given local geographical names.

We note that palaeomagnetic–stratigraphic comparisons in the USSR are based almost exclusively on palaeontological data. Unfortunately good stratigraphic sections are not usually satisfactory for palaeomagnetic investigations ; on the contrary, those favourable for defining palaeomagnetic research sections do not have fossils. This makes it difficult to correlate regional palaeomagnetic columns, in order to estimate accurately the length of R zones and to draw up an integrated palaeomagnetic time scale. For example, the R zones in Santon and Campan are likely to be the same as the Kuldijinian zone, because in each section we see only one zone in this time interval. The same may be true for Gatan, Chagyl and elsewhere. In Central Asian sections, correlation is difficult because of scarcity or absence of fauna.

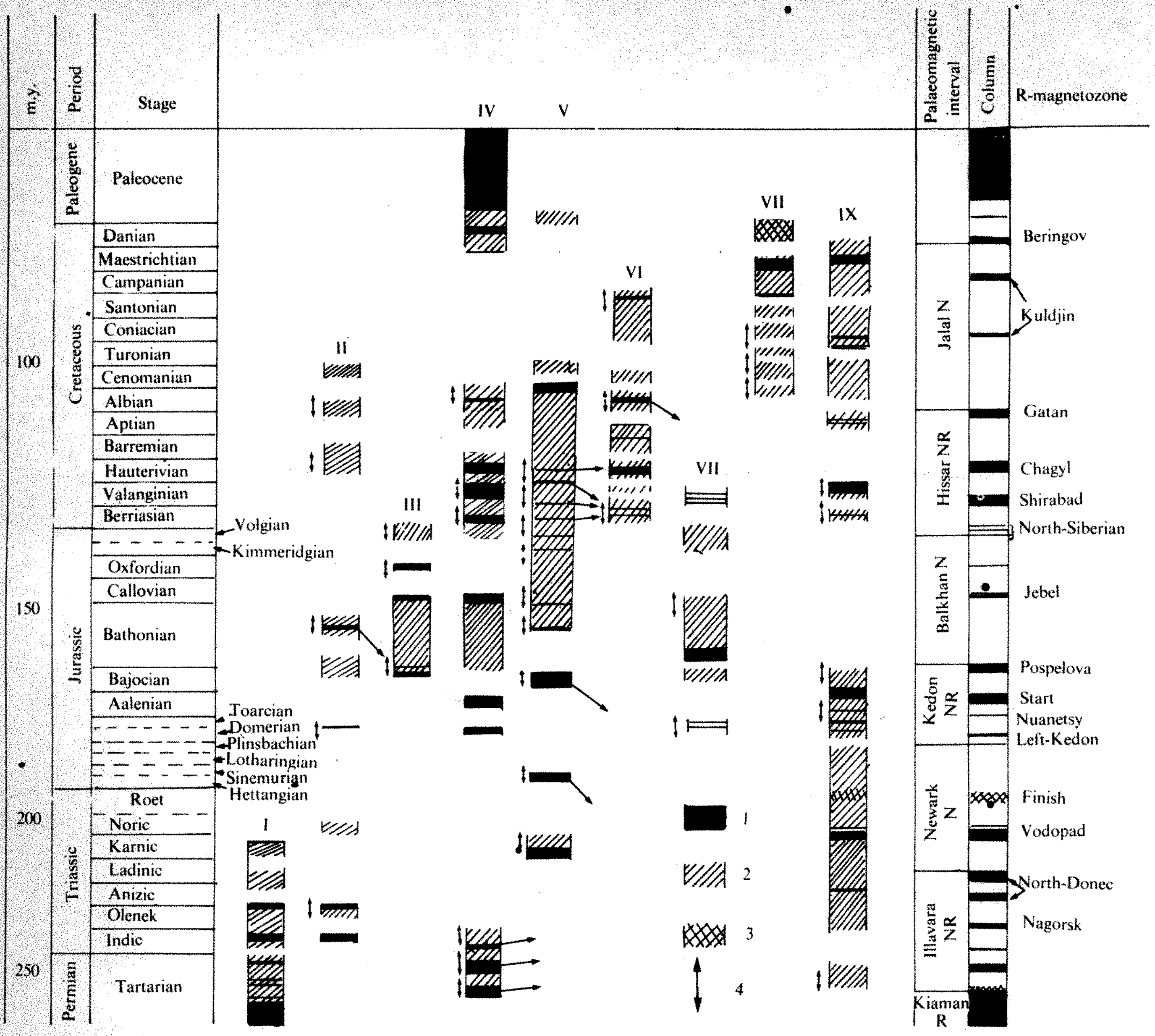

Fig. 1 Correlation of regional palaeomagnetic Mesozoic scale of the USSR. I, Russian Platform[5,6,8,10]; II, Donbas and Crimea[4,8,13,16]; III, Azerbaidjan[3]; IV, Turkmenistan and Western Kazakhstan[8,11,13,15]; V, Tadjikistan, Tajic Depression[3,6]; VI, Fergana[3,9,14]; VII, north Siberia[3,12]; VIII, Sakhalin[3]; IX, north-east Asia[2,3]; X, palaeomagnetic Mesozoic scale of the USSR. 1, Palaeomagnetic R zones; 2, N zones; 3, zones of mixed polarity; 4, approximate position of boundaries or duration of palaeomagnetic zone.

An analysis of the integrated Mesozoic palaeomagnetic column shows, first, that in Mesozoic sediments, natural remanent magnetization of normal polarity prevails; corresponding to more than 80% of the time in the Mesozoic era, the geomagnetic field had normal polarity.

Second, there may be as many as twenty palaeomagnetic R zones; their duration runs from 0.5 to 3 or 4 m.y. with an average of about 1.5 m.y. The duration of N zones runs from 0.5 to 20 m.y.

Third, distribution of R zones in time is not even; there is a tendency for interchanging "thicks" and "thins" of geomagnetic field reversals. The intervals last 20–40 m.y. Beginning with the middle of the Tartarian stage of late Permian (after the Kiaman R interval) and finishing in the Palaeocene, seven palaeomagnetic intervals were obtained (Fig. 1). Two intervals—Illavana and Jalal—are the most reliable.

Our suggested scheme is not complete. It is possible that new R zones will be discovered and that some uncorrelated zones will be liquidated before an exact column is determined, but we believe that the overall picture of the distribution and total duration of palaeomagnetic intervals and zones will not change.

We have summed up the initial stage of accumulating palaeomagnetic data for the Mesozoic in the USSR. In order to draw up the world palaeomagnetic scale for Mesozoic and other eras it is necessary: that detailed palaeomagnetic investigations be made using all available modern methods of the most complete and uninterrupted sedimentary and volcanogenic sequences in a number of world regions to draw up palaeomagnetic stratotypes; that stratotypical sections be dated by different methods (radiological, palaeontological); and that a nomenclature of palaeomagnetic stratigraphy be worked out.

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Ancient Metamorphic-migmatite Belts of the Brazilian African Coasts

ABOUT 150 m.y. ago, a successful rift formed which led to the separation of present day South America from Africa. Many types of rocks from Precambrian migmatites to Lower Cretaceous evaporites[1] match across the junction of rifting; but why do continental masses rift where they do? The answer could lie in purely random phenomena, but time after time ancient trends and structures seem to control later events. If events in the mantle are random, perhaps they lead to successful amplification only when they interact with certain structural situations in the continental crust. Only recently have sufficient data become available on the basement rocks of the Atlantic coasts of Africa and Brazil to allow a preliminary synthesis. But it seems certain that the rifting followed an ancient intercratonic structural trend (mobile belt) with a complex history of metamorphism and magmatism. The rifting process was not random.

The general structure of the two continents (Fig. 1) is well known[2,3]. Stable continental nuclei with ages in the 3,000 m.y. range are surrounded by younger metamorphic belts. The older belts tend to be in the granulite facies of metamorphism and are associated with charnockites and migmatites. Metamorphism in these is of the Abukuma type and their mineralogy suggests thermal gradients of the order of 60° C km^{-1} or more. These ancient metamorphic belts are followed by many younger belts with typical Barrovian facies series indicating lower thermal gradients. In fact, the trends could be correlated with a general decrease of thermal gradients with time of magnitude 0.03° C/m.y. Along the Atlantic coasts of South America and Africa there is widespread development of ancient high temperature/low pressure metamorphic rocks and it is along this belt that parting occurred.

Experimental studies of granite production[4,5] indicate that the granulite-charnockite-migmatite association represents a situation at the base of the acidic crust where partial melting occurs. Such ancient basement crust has been uplifted to form the zone of continental splitting. It seems reasonable that the large heat fluxes needed for migmatization may be associated with the rise of basaltic magma from the upper mantle. Thus in forming the high grade assemblages one may expect a series of steps such as the following.

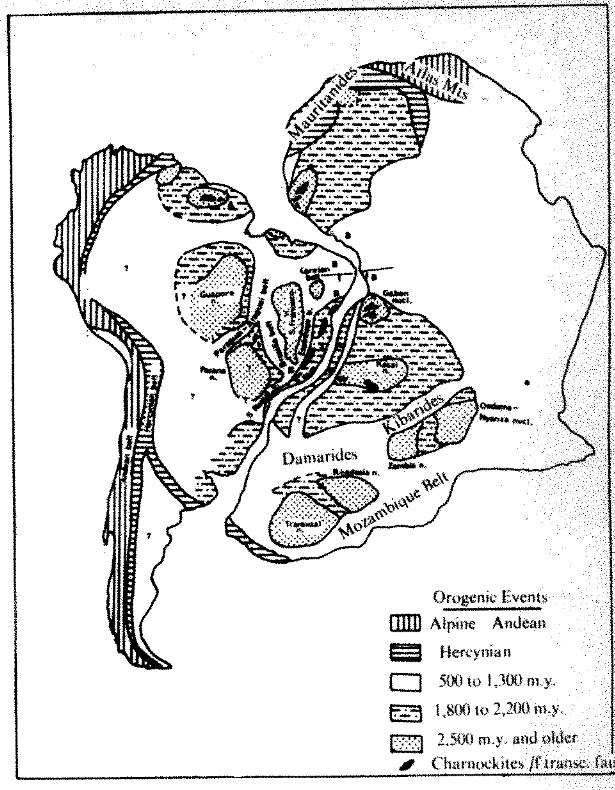

Fig 1 Tectonic regions of Africa[2] and Brazil[3]. H, High pressure; B, intermediate pressure (Borrovian); A, low pressure (Abukuma).

(1) The creation of a thermal anomaly in the upper mantle (plume) which leads to surface basalt eruption and general heating of the crustal region.

(2) The fusion of the base of the crust and the start of acid plutonism and volcanism.

(3) Once the base of the crust becomes "sticky" on a large scale, basalt cannot be extruded but instead it flows beneath the low viscosity crust. This basalt may differentiate to produce peridotite-anorthosite complexes because of the very long cooling time in a hot environment. Basalt injected at even greater depth could crystallize to eclogitic complexes. We thus expect the observed association of basaltic differentiates and anorthosites with the migmatite-charnockite regions.

The arguments presented below indicate that separation along a zone of uplifted granulitic basement may not be accidental. We imagine that mantle thermal anomalies (plumes) can arrive under any crustal section by random processes. If a plume arrives beneath a cratonic region with a thick granitic layer we might expect a series of events as follows.

(a) Dyking of the crust (some spreading and uplift) and surface eruption of basalt.

(b) Gradually the base of the crust is heated and partial melting commences.

(c) Granitic plutonism and acid volcanism commences. When the base of the crust has a large melt fraction and hence a low viscosity, basalt penetration ceases.

(d) Basalt from the upper mantle is injected beneath the crust. At high levels it differentiates perfectly (possibly with extensive contamination) to produce rocks of the anorthosite-peridotite suite. At lower levels eclogite forms.

(e) Extensive development of eclogite loads the overall active zone and downwarps the upper mantle melting zone.

(f) Plumes migrate laterally and the craton is preserved but thickened at the base with basaltic material. It is for this reason that ancient cratons tolerate successions of basaltic invasions but still survive. The plumes are transient.

If a similar plume arises under a mobile belt where granulitic basal crust underplated by basalt is uplifted, flood basalts and dyking will occur. There is insufficient high level granitic phase to cut off basalt extrusion. A successful spreading ridge results and the continent splits. We consider that such models may explain why old mobile belts become the sites for future continental fission and that the type of high grade metamorphic rocks on the Atlantic margins of South America and Africa is not accidental. Under zones of thick granitic crust, plumes may be transient and will persist only under regions of thin acid crust, an ocean ridge type situation where most basaltic magma is injected near the surface.

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High Resolution Map of NGC1265

THE radio sources associated with NGC1265 and IC310 have "head-tail" structures with the heads coinciding with the optical galaxies[1]. Ryle and Windram suggested[1] that both radio sources were ignited by a relativistic particle wind from the nearby Seyfert galaxy NGC1275. Hill and Longair[2] drew attention to further examples of galaxies in clusters with the same peculiar radio morphology.

This "interacting galaxies" hypothesis has been criticized[3], and it has been suggested that galaxies such as NGC1265 are radio sources in their own right, not causally connected with any other galaxy. The elongated radio tails are then explained as trails left as active radio galaxies plough through the cluster medium. Here we present a high resolution map of NGC1265 which provides further evidence in favour of the "radio trail" hypothesis and thereby argues for the existence of an intracluster medium.

The observations were made with the Westerbork synthesis radio telescope at 5 GHz during 4 sets of 12 h in December 1972 and January 1973. Interferometer baselines ranging in length from 36 m to 1,458 m in steps of 18 m were used. Our resulting map has an elliptical synthesized beam 6×10 arc s to half power, with a first diffraction grating ring whose size is 11×17 arc min. The system temperature was 200 K and the bandwidth 4 MHz, giving an r.m.s. noise on the map equivalent to 0.6×10^{-29} W m^{-2} Hz^{-1} per synthesized beam.

In Fig. 1 we show the new 5 GHz map superimposed on the blue Sky Survey print. A diffraction grating ring due to the nearby strong radio galaxy NGC1275 confused part of our original map, but the influence of this source has been removed using a point source subtraction program. For comparison, the lower resolution 1.4 GHz map of NGC1265 is given in Fig. 2, also superimposed on the optical photograph. In both cases only the most intense region of the source near the optical galaxy is shown because the fainter part of the tail is mostly below the noise level at the full resolution of the 5 GHz system.

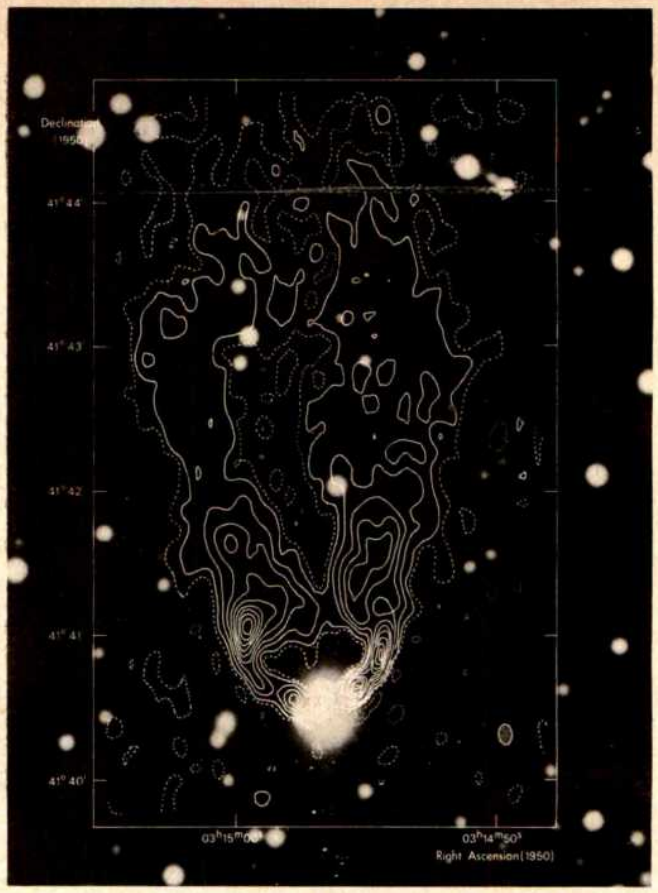

Fig. 1 Westerbork 5 GHz map of NGC1265 superimposed on the blue Palomar Sky Survey print. Continuous contours are plotted at intervals of 2.5 m.f.u. per synthesized beam from 2.5 m.f.u. to 22.5 m.f.u. Dashed and dotted contours indicate the 1.25 m.f.u. and -1.25 m.f.u. levels respectively. No correction is made for the effect of the 10 arc min primary beam centred at RA 03 h 15 min, dec. 41° 45′. The shaded ellipse corresponds to the half-power synthesized beam.

The superpositions, accurate to ~2 arc s near the nucleus of NGC1265, were carried out using optical positions of two nearby stars supplied by Mme Heidmann. Bertola and Perola[4] have found optical emission out to 100 arc s from the nucleus so the optical image of the galaxy covers a large part of the 5 GHz map.

There are several striking characteristics of the map: the semicircular shape of the radio head; the discrete components within that semicircle; the prominent central component near the nucleus of the galaxy; the deep well behind the head; the two ridges of emission behind the well which stretch far down the tail; the central connexion behind the well which forms a bridge between these two ridges; and the general symmetry of the source.

It is difficult to envisage how such a radio source could be ignited from NGC1275 or any other galaxy; we shall interpret these features only in terms of the "radio trail" hypothesis. The simplest version of this hypothesis[6] is shown schematically in Fig. 3 with the 5 GHz contour diagram. Here NGC1265 is assumed to be travelling with a transverse velocity ν_g in the direction indicated, recurrently ejecting pairs of radio-emitting blobs with transverse velocity ν_e into the intergalactic medium.

The shape of the head and the width of the tail are determined by the ratio ν_e/ν_g, by the angle between ν_e and ν_g and by the deceleration of the components. The latter depends on the component masses and cross sections and on the density of the intergalactic gas. A line joining components A_1 and A_2 (Fig. 3) would be almost perpendicular to the symmetry axis of the source, implying that ν_e and ν_g are oriented approximately at right angles. (This is probably fortuitous because other head-tail sources such as 3C129 and IC310 show no evidence for the same alignment.) In this case a good fit to the shape is given by values of ν_e/ν_g ranging from 1 to 3. The predicted trajectory for $\nu_e/\nu_g=2$ is shown in Fig. 3. NGC1265 has a radial velocity of ~2,300 km s^{-1} with respect to the mean of the Perseus Cluster[7] and we assume that the transverse velocity, ν_g, is of that order. Our observations therefore imply injection speeds of a few thousand km s^{-1}, comparable with those now believed to occur in simple double radio galaxies[8].

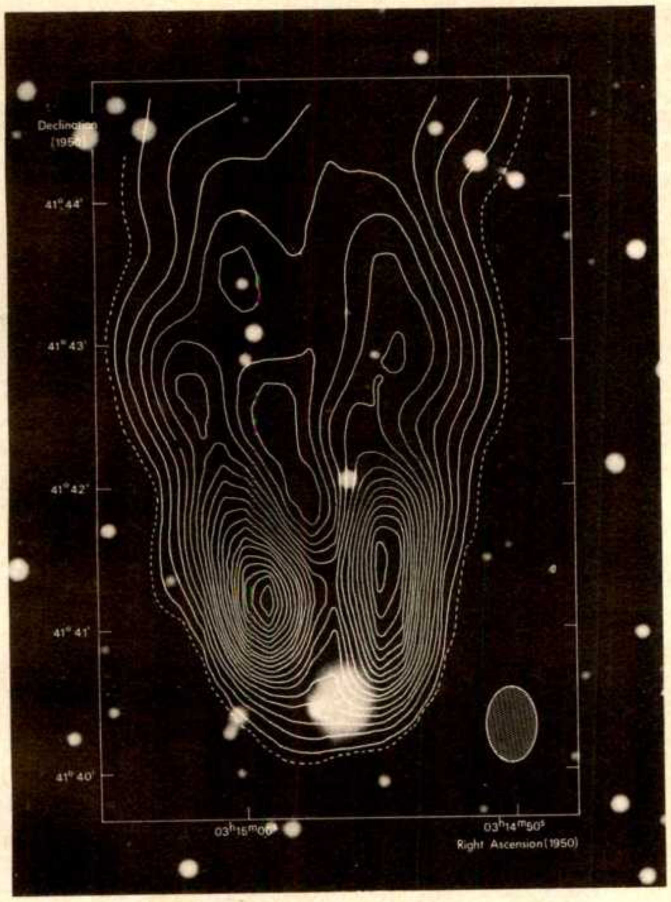

Fig. 2 Westerbork 1.4 GHz map of NGC1265 superimposed on the blue Palomar Sky Survey print. Continuous contours are plotted at intervals of 18.5 m.f.u. per synthesized beam from 18.5 m.f.u. to 351.5 m.f.u. Dashed contours indicate the 9.25 m.f.u. level. No correction is made for the effect of the 36 arc min primary beam centred at R.A. 03 h 15 min, dec. 41° 38'. The shaded ellipse corresponds to the half-power synthesized beam.

The discrete components in the radio emitting arc show that the ejection is repetitive. Assuming NGC1265 is at 60 Mpc and $\nu_g=2,000$ km^{-1}, $\sim 4\times 10^6$ yr is the typical period between principal outbursts. Each of these requires a minimum energy of 10^{55} erg. The length of the tail at 1.4 GHz implies continual activity for at least 10^8 yr.

The front central component of Fig. 1 is absent from Fig. 2. It has a flux density of $(27\pm 3)\times 10^{-29}$ W m^{-2} Hz and lies 4 arc s south-west of the optical centroid measured by Heidmann. Because this is within the errors of the optical measurement we presume that the component is associated with the nucleus of NGC1265. A comparison with the lower resolution Westerbork 1.4 GHz (Fig. 2) and Cambridge 2.7 GHz (ref. 9) maps shows that the nuclear component has a flatter spectrum than the source as a whole, indicating that it is partially opaque, compact and presumably active. The flat spectrum nuclear components in NGC1265 and 3C129 resemble those already known to occur commonly in classic double radio galaxies (such as 3C390.3, ref. 10, and 3C310, G. K. M., and H. L., unpublished) and provide further evidence that similar activity is occurring here.

A possible faint emission ridge (T) stretches across the well towards the nuclear component. It is tempting to interpret this as a trail of the nucleus itself which is simmering between major eruptions reminiscent of the variable galactic source associated with Cyg X-3 (ref. 11).

The well enclosed by the radio head can be explained because the component pairs A_1A_2 and B_1B_2 are presumably young, still highly confined by the ram pressure of the medium, and have not begun to diffuse backwards along their trajectories. The more relaxed ridges of emission in the tail and the central connexion between them are formed by older components that have reached the expansion stage. The contour map is somewhat deceptive here because it suggests that the connexion occurs only just behind the well. But the bridge between the ridges may be present all along the tail because even if it continued at the same relative intensity it would fall below the noise level of the map.

The profiles C_1C and C_2C are very similar to intensity profiles along the major axes of many double radio galaxies. The steep outer and gentle inner gradients suggest that the components evolve in the same way as those in double sources. Initially they are confined by ram pressure, but soon the rear portions of the components expand back along their own trajectories, where they meet least resistance. This expansion may form a bridge, well known in double sources and present here behind the well. Ultimately the components are stopped and fade away as they expand against the static pressure of the medium. The contrast between the outer and inner gradients then slowly disappears. The detailed structure may then be dominated by the magnetic field of the galaxy as described in the magnetospheric model[6].

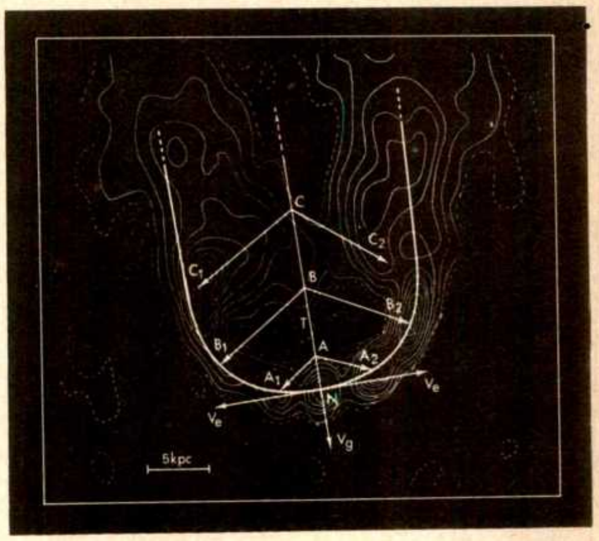

Fig. 3 Schematic diagram of a simple "radio trail" model superimposed on the 5 GHz contour map of NGC1265. The galaxy moves with transverse velocity ν_g recurrently ejecting pairs of radio emitting blobs (A_1, A_2), (B_1, B_2), (C_1, C_2) with transverse velocity, ν_e. We note the presence of a possible faint emission ridge T.

The source symmetry is also comparable to that apparent in many double radio sources. The flux density ratios for the different pairs are within a factor ~3 and the luminosity from one pair to the next does not differ greatly. In addition the width of the tail is quite constant throughout its length. Thus successive major events repeat at very similar power levels and ejection velocities. The phenomenon that we witness in NGC1265 is extremely informative because it spatially separates these different events in time. In the usual double radio galaxies, the effects of such repeated eruptions would be superimposed and hence could not be temporally ordered. It also demonstrates conclusively that the nucleus of this galaxy can recover from and repeat an energy release of $\sim 10^{55}$ erg after a few million years.

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Absolute Frequency Measurement of the R(12) Transition of CO_2 at 9.3 μm

THE frequency of a CO_2 laser stabilized to the R(12) transition of CO_2 has been measured with an accuracy better than one part in 10^9. This is part of an experiment at the National Physical Laboratory to determine the speed of light to the full accuracy of the krypton-86 length standard[1].

Our result for the frequency of the CO_2 R(12) transition is

$$\nu = 32{,}176{,}079{,}482 \pm 28 \text{ kHz}$$

The provisional error comprises a random error of 4.2 kHz and possible systematic effects amounting to 27.5 kHz combined as the root sum of squares throughout. Further studies of these effects may reduce the error, which will be discussed in more detail elsewhere.

Comparison of the CO_2 laser frequency with the caesium standard at 9 GHz is achieved by harmonic generation and mixing of radiation from microwave, submillimetre wave and infrared sources, using point contact devices. The apparatus is an extension of that recently described for measurement of a stabilized H_2O laser frequency at 28 μm (ref. 2). The CO_2 laser was stabilized to a saturated absorption dip observed using the 4.3 μm fluorescence[3] from an external CO_2 gas cell. The following three frequencies were measured concurrently. (i) The beat frequency between the CO_2 laser and the 3rd harmonic of a free-running 10.7 THz (28 μm) H_2O laser; (ii) the beat frequency between the H_2O laser and the 12th harmonic of a free-running 891 GHz (337 μm) HCN laser; and (iii) the HCN laser frequency via a klystron phase locked to the laser by fiftieth harmonic mixing in a Josephson junction.

A total of 480 readings in forty-eight sets of ten were obtained on five different days over a period of two months. Apart from the initial day (forty measurements) there were about 100 measurements per day with a standard deviation of a single reading near 60 kHz. Each set of ten was averaged and the standard deviation of the mean of these forty-eight averages was 4.2 kHz. The means of the four principal days were consistent to ±4 kHz.

The chief causes of systematic error were: (a) possible asymmetry in the HCN laser spectrum causing a difference between time-averaged counting and the centre of the beat spectrum as observed and measured on a spectrum analyser; (b) uncertainties in the offsets produced by the servo-control system which locked the CO_2 laser to the dip in the saturated absorption signal from the CO_2 gas cell; (c) thermal drift of the HCN laser frequency during the period of measurement (of the order of 1 s); (d) uncertainties in the relation of the local working frequency standard to the caesium standard.

After completion of our measurements and the foregoing analysis the result for the frequency of the CO_2 R(12) transition was communicated to the meeting of the Comité Consultatif pour la Définition du Mètre (June 14), and a comparison was made with the R(10) transition frequency measurement of K. M. Evenson *et al.*[4] using a value for the R(12)–R(10) difference frequency recently determined at the National Bureau of Standards, Boulder. The agreement was within 3 parts in 10^{10}, and thus confirms one part of the frequency measurement by Evenson *et al.* in their determination of the speed of light[5].

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Observation of Electron Swarms produced by Laser Light

OBSERVATION of the displacement current caused by the motion of charge carriers in a discharge gap can yield quantitative information on many basic processes[1], such as ionization, electron attachment and charge carrier mobilities. A relatively large number of charge carriers is, however, required to produce a signal which exceeds the high inherent noise level of any wideband detection system by a sufficient margin. Hitherto, it was necessary, except in one or two special cases, to rely on gas amplification to raise the electron current to an observable level; this is only possible, however, when ionization dominates attachment of electrons to neutral molecules. The number of initial electrons required is particularly high when measurements in electronegative gases (high voltage insulants such as SF_6 and air) are to be made over the technically important range of low ratios of field strength to pressure for which the electron loss by attachment is at least as probable as the production of additional electrons by ionization.

In order to apply relatively simple methods of electron current pulse shape evaluation, the primary electrons must be released from the cathode within a very short time; on the other hand, a high light intensity is required to produce a reasonable number of primary electrons. Attempts have been made to produce such a large number of primary electrons by ultraviolet light flashes (ref. 2 and references in ref. 1). With spark light sources, however, those two requirements contradict each other. Higher energy input tends to lead to a longer duration of the light emission; in particular, the light emission frequently shows a very long "luminosity tail" of lower intensity which can be troublesome in gas discharge studies. Attempts have been made to eliminate the tail by means of an electro-optic shutter[3], but the number of photoelectrons generated from normal cathodes by the shortened ultraviolet pulse (10^3) is far too small for many investigations. When the luminosity tail was not suppressed, primary electron numbers of about 10^6 within 20 ns were obtained from specially prepared cathodes in certain gases.

To overcome the drawbacks of spark light sources, we have used a Q-switched ruby laser with frequency doubling to generate an intense, short ultraviolet light pulse which has no tail. The fundamental and second harmonic frequency light beams are passed into a liquid filter to remove the red light which can cause thermionic emission. The ultraviolet beam is then expanded to illuminate a large central area of the cathode of a homogeneous field discharge gap. In this way, more than 10^8 photoelectrons can be generated within a well defined time interval less than 20 ns long. The displacement current set up by these electrons moving through the discharge gap is sufficiently high to permit direct recording with high time resolution even when the applied field is comparatively low. Thus the region of low field strength to pressure ratio, in which there is little or no ionization or even predominant attachment, becomes accessible for time-resolved current observation. In fact, measurements at ratios as low as 4 V m N^{-1} (5 V $torr^{-1}$ cm^{-1}) have proved possible in CO_2 and permit determination of mean electron energies from the very pronounced influence of diffusion upon the pulse shape.

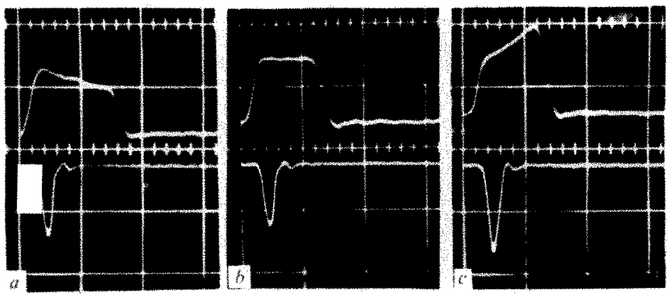

Fig. 1 Electron current pulses in carbon dioxide (pressure 12.8 kN m^{-2}, 96 torr) at different ratios of field strength to pressure: *a*, 10; *b*, 19; *c*, 21 V m N^{-1} (14, 26, 28 V cm^{-1} $torr^{-1}$). Top traces: current at 150 μA per principal division. Bottom traces: laser light intensity, time axis offset by 25 ns. Time scale in all cases 100 ns per principal division. For the conditions of *a*, attachment predominates ($\alpha-\eta=-31$ m^{-1}); for *b*, attachment and ionization balance each other; for *c*, ionization predominates ($\alpha-\eta=+44$ m^{-1}).

Typical current oscillograms for an electronegative gas are shown in Fig. 1. They allow the immediate determination of electron drift velocities and thus mobilities (from the pulse duration) and of the effective ionization coefficients α-η, where α is the ionization coefficient and η the attachment coefficient. Trace (*a*) shows clearly the gradual reduction in the number of electrons due to attachment; the attachment coefficient η is here greater than the ionization coefficient α. The resulting negative ion current does not show in the oscillogram because of the much lower mobility of negative ions. A constant electron current which indicates equal values of ionization and attachment ($\alpha=\eta$) is shown as trace (*b*). Quite small changes in the field strength to pressure ratio ($<2\%$) lead to a clearly discernible slope of the roof of the current pulse. Under the conditions of trace (*c*) the electron current is amplified by the predomination of ionization over attachment.

The observation of ion currents in all these conditions is well within the capabilities of the system and will yield all the information which could hitherto only be obtained in this way at the higher ratios of field strength to pressure. Such information and further details of parameters obtained from electron current pulse evaluation will be reported elsewhere.

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BIOLOGICAL SCIENCES

Genetic Transfer of the Stable L Form State to Intact Bacterial Cells

QUANTITATIVE mass conversion of bacteria to protoplasts and unstable L phase variants and the reverse process are probably not mutational events. The transition from unstable L phase variants to stable L phase variants, however, probably reflects a fundamental genetic change, although this is still in dispute[1]. Increasing circumstantial biochemical data support this but genetic evidence is virtually non-existent. Several stable L phase variants, when compared with the protoplasts or bacteria from which they were derived by non-mutational induction procedures, are lacking in certain wall components[2,3] and part of the DNA[4], and possibly defective in stages of wall biosynthesis[5,6], and to possess altered membrane constituents[7,8], all of which may reflect an inability to carry out proper wall formation.

We used transformation to determine if the stable L state could be transferred to intact bacteria to result in the phenotypic expression of stable L forms. DNA from a stable L phase variant derived from *B. subtilis* 168 *trp* C2 (ref. 9) was isolated[10] and used for transformation[14]. Saturating concentrations of DNA were used to transform competent cells of two recipients: M22 *pur* A16, *leu*-8, *met* B5, *ile*-1, and a streptomycin-resistant spontaneous mutant of 167 *trp* C2, *thy*, both of which were derived from *B. subtilis* 168 (ref. 11). Recombinants which were prototrophic for adenine and thymine were selected on DP agar plates (DPA)[9], containing 0.5 M sodium succinate as an osmotic stabilizer and devoid of both horse serum and methicillin. A chemically defined medium SD (ref. 9), appropriately supplemented, was used to score the *pur*$^+$ recombinants for retention of unselected amino acid markers. As L form colonies cannot be replica plated, individual L form colonies were excised from the isolation plates with a scalpel, mashed in sterile SD liquid medium, and aliquots of the suspension were spread on the appropriate plates to screen for unselected markers. Representative results are recorded in Table 1.

Transformation frequencies of 0.1–0.25% were routinely obtained for adenine recombinants. Three types of colonies were present on the initial selection plates: (1) *pur*$^+$ bacterial colonies; (2) *pur*$^+$ L forms (Fig. 1); and (3) a background growth of tiny colonies consisting of rods (Fig. 1*a*, *b*, arrows). The appearance of the latter colonies was probably the result of trace amounts of adenine contamination in the base medium. These tiny colonies presented difficulties in obtaining pure growth of many of the L forms on subculture, but it could be demonstrated that most of the L form transformants retained the auxotrophic markers of the recipient bacterium.

Transformation frequencies for thymine recombinants were 0.025%, 0.01% and 0.03%. Only two types of colonies were

Table 1 Transformation of the Stable L Form State to Intact Bacterial Cells

Donor	Recipient	Selected marker	Transformant colonies ml^{-1}	Co-transformation Marker	%
168 *trp* C2, S1f-1	M22 *pur* A16, *leu*-8, *met* B5, *ile*-1	*pur*$^+$	1.74×10^6	*leu*	14
				S1f-1	9
168 *trp* C2, S1f-1	167 *trp* C2, *thy str*	*thy*$^+$	1.66×10^6	*str*	8
				S1f-1	15

* S1f-1, phenotypic expression to denote stable L form, in accordance with the terminology recommended by Young and Wilson[16] for morphological mutants.

present on the initial selection plates: (1) *thy*$^+$ bacterial colonies, and (2) *thy*$^+$ L forms. L forms obtained on subculture of an initial *thy*$^+$ L form recombinant are represented in Fig. 2. Scoring of the L form recombinants for streptomycin resistance was performed on DPA containing 1,000 μg ml^{-1} streptomycin. These L forms were also tested for their stability by their ability to grow as L forms on DP medium containing 2.5% agar and DP medium supplemented with 25% gelatin. The results are recorded in Table 2.

In all the transformation experiments performed the number of L forms obtained represented approximately 10% of the total number of transformants. Inoculation of the recipient bacterial cells alone on DPA never resulted in the appearance of L forms. Further proof that the L forms were derived from the recipient cells was demonstrated by the retention of recipient markers. It may be concluded therefore that the L form colonies arose as a direct result of genetic transformation. The stability of the L form transformants was demonstrated by their inability to revert to the classical bacterial phase on hard agar or medium supplemented with 25% gelatin[12,13,15]. Our study clearly demonstrates that this stable *B. subtilis* L phase variant, eventually obtained from initial treatment of the parent

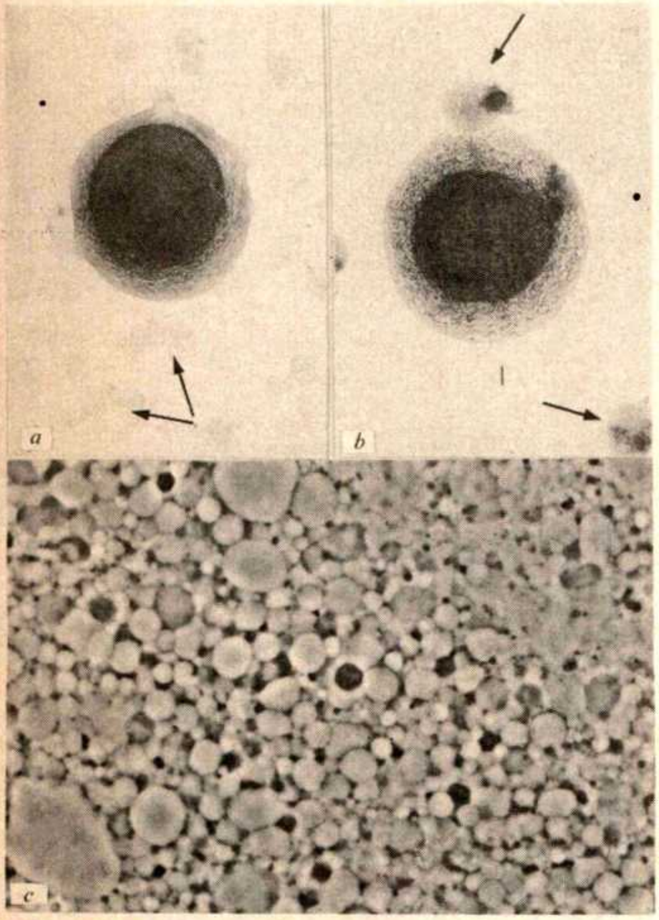

Fig. 1 Individual *pur*$^+$ recombinant L form colonies on initial selection plates. *a* and *b*, Low power photomicrographs reveal L form colony morphology: a dense centre surrounded by a vesicular periphery; magnification ×63. The arrows point to background growth of small colonies, consisting of rod cells, which arose probably as a result of trace amounts of adenine in the base medium. *c*, High power photomicrograph of L phase variant cells in an L form colony; magnification ×1,000.

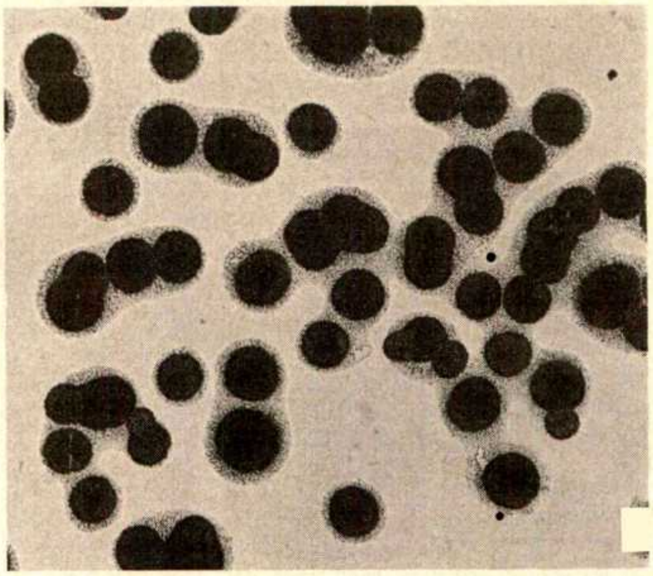

Fig. 2 L forms obtained on subculture of an initial *thy*$^+$ L form recombinant.

Table 2 Scoring of L Form *thy*$^+$ Recombinants for Streptomycin Resistance and Stability

L Form *thy*$^+$ recombinants	Streptomycin resistance	Reversion to bacterial phase 2.5% agar	25% gelatin
AA1	+	0	0
AB1	+	0	0
AC2	+	0	0
AC3	+	nd	0
CA5	+	0	0
CB2	+	nd	nd
CC1	–	nd	0
CC3	+	0	0
CC4	–	0	nd
C41	+	0	0
Control L phase variant	–	0	0

–, No growth; 0, no reversion, growth as L forms; +, growth; nd, not done.

bacterial cell population with lysozyme, is a mutant and that the characteristic responsible for the stable L state can be transferred to an intact bacterial cell with the resultant recovery of a stable L form

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Cascade Activation of Genome Transcription in Wheat

TRANSCRIPTIONAL events are arrested in developing plant seeds when maturation is completed The RNA synthesis may be resumed when suitable changes in the environment make it possible for the seed to germinate It is not known, however, how early and in what order the synthesis of cellular RNA species is activated in response to the stimulus to germinate Our previous observations[1,2] indicate that RNA synthesis is triggered almost immediately before the activation of protein synthesis *in vivo* but other reports[3-5] suggest that RNA synthesis remains repressed for many hours after germination starts Further attempts to establish the time course of RNA synthesis in germinating wheat embryos were therefore undertaken

The seeds of wheat, *Triticum aestivum*, were labelled with ^{14}C-uridine and germinated as described (Fig 1) The precursor was incorporated into the embryo RNA from the onset of germination, but the rate of incorporation was not constant throughout the investigated period (Fig 1) There was a rapid phase of RNA synthesis (0 to 3 h), followed by a levelling (3 to 12 h) after which the synthesis resumed linearly The levelling could not result from a dilution of the precursor by the endogenous uridine The considerable drop in specific radioactivity of uridine was found to occur in the embryo only 12 h after germination started

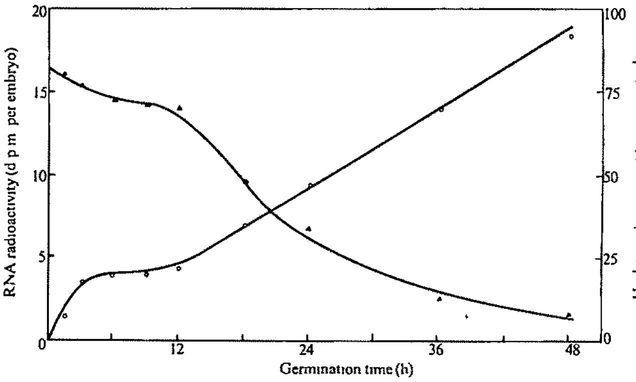

Fig. 1 Time course of ^{14}C-uridine incorporation into wheat embryo total RNA during germination A sample of 250 wheat grains was surface sterilized with 2% NaClO, immersed in 10 ml of ^{14}C-uridine solution (0 03 μCi ml^{-1}, 0 6 μCi μmol^{-1}) at 2° C for 8 h and then allowed to germinate at 22° C After the requisite germination period, embryos were separated manually from the remaining parts of the grains and used for the isolation of total RNA and uridine Total radioactivity of the isolated RNA (○) and specific radioactivity of the isolated uridine (△) were then determined[1]

The biphasic time course of uridine incorporation (Fig 1) seems to indicate that RNA synthesis is activated in the germinating wheat embryos in a stepwise manner The first activation step results, probably, in only limited RNA synthesis This initial activation begins immediately after germination starts, and is apparently completed within the first 3 h Further activation does not begin until 12 h after the start of germination The second activation step probably leads to the full activation of cellular RNA synthesis

It seemed desirable to compare RNA species synthesized in conditions of limited activation with those appearing after the activation is fully completed Distribution of the newly synthesized (labelled) polynucleotides among mRNA, rRNA and tRNA fractions was therefore studied as a function of the germination time The α variant mRNA fraction was isolated according to the method of Weeks and Marcus[6] After preliminary screening experiments, the methods of Caldwell and Henderson[7] and Delihas and Staehelin[8] were chosen for the isolation of rRNA and tRNA fractions, respectively The recoveries of the added labelled rRNA and tRNA were checked and found to be satisfactory (75 to 85%) It was shown that the initial activation of RNA synthesis results in the labelling of mRNA fraction only (Table 1) The second activation step probably corresponds to the initiation of rRNA synthesis Significant radioactivity appeared in this fraction after 12 h germination and increased considerably thereafter Soon after the rRNA synthesis began, the third activation step, manifested by the labelling of the tRNA fraction, occurred The tRNA fraction contributes little to the total RNA radioactivity (15% after 24 h germination) and, for this reason, the last activation step cannot be distinguished from the incorporation curve (Fig 1)

The sequential labelling of mRNA, rRNA and tRNA fractions may suggest an ordered derepression of the genome, provided that the mRNA fraction does not contain rRNA precursor (or tRNA precursor) molecules To distinguish between mRNA and rRNA precursor molecules, the nucleotide composition of the newly synthesized RNA was determined with the use of ^{32}P$_i$ as the precursor It was found that the early RNA is rich in U+G and is unlike the total RNA of the dry or germinated embryos The low CMP content (14 8 mol%) does not indicate an early rRNA synthesis and does not confirm the recent finding of Chen *et al*[9] although the base composition found here for the early synthesized RNA is similar to that of RNA present in the messenger fraction of the wheat embryo[2] The early RNA differs from most mRNAs in its low AMP content Histone mRNAs, however, do not contain poly (A) sequences[10,11] A need for histone mRNA synthesis in the embryos may be expected, as a burst of histone synthesis has been observed in a similar system[12]

The mRNA fraction, isolated from wheat embryos according to the method of Weeks and Marcus[6], is obtained as a

Table 1 Incorporation of ^{14}C-Uridine into mRNA, rRNA and tRNA and Fractions of Germinating Wheat Embryos

Germination time (h)	Messenger fraction (mg per 100 embryos)	Messenger fraction (d.p.m. mg^{-1})	Ribosomal fraction (mg per 100 embryos)	Ribosomal fraction (d.p.m. mg^{-1})	Transfer fraction (mg per 100 embryos)	Transfer fraction (d.p.m. mg^{-1})
0	0.05	<50	1.30	<10	0.60	<10
0.75	0.04	1,050	1.35	<10	0.62	<10
1.5	0.04	3,800	1.30	<10	0.62	<10
3	0.05	7,350	1.23	<10	0.60	<10
6	0.06	6,100	1.26	<10	0.51	<10
12	0.06	4,250	1.32	190	0.40	<10
24	0.08	1,400	1.58	430	0.45	360
48	0.08	850	1.77	710	0.73	740

RNA (amount and radioactivity)

Wheat grains were labelled and germinated as described in the legend to Fig. 1. The RNA fractions were isolated from the embryo moiety of the grain according to methods quoted in the text.

nuclear ribonucleoprotein complex, sedimenting at 39,000g. When the pellet was resuspended in the extraction buffer[6], layered on a 10 to 30% sucrose gradient and centrifuged at 85,000g for 2 h, the material absorbing at 260 nm sedimented heterogeneously between 40S and 200S. The isolated material was rapidly degraded to 40S particles after 6 h storage at 0° C. The 40S particles were composed of protein and RNA in a mass ratio of 4:1. Only the RNA component was radioactive in the 40S RNP particles isolated from embryos labelled with both ^{14}C-uridine and ^{14}C-leucine and germinated for 3 h. This indicates that the newly synthesized RNA combines, within the cell nucleus, with a pre-existing protein component. The resulting RNP particles may be compared with informosomes known from other studies[13]. Although the ultimate characterization of the mRNA fraction must await the identification of the proteins that it codes for, all the data so far available are consistent with the assumption that this fraction is similar to nascent mRNA-protein complexes known to occur commonly in other eukaryotic cell nuclei.

Table 2 Nucleotide Composition of Total and Newly Synthesized RNA of Germinating Wheat Embryos

Germination time (h)	Total RNA AMP	Total RNA GMP	Total RNA CMP	Total RNA UMP	Newly synthesized RNA AMP	Newly synthesized RNA GMP	Newly synthesized RNA CMP	Newly synthesized RNA UMP
0	23.5	31.1	24.8	20.6	—	—	—	—
3	21.2	32.0	24.3	22.5	11.4	36.5	14.8	37.3
48	22.7	30.9	24.8	21.6	22.8	29.3	25.8	22.1

Nucleotide proportions (mol %)

Wheat grains were labelled and germinated as described in the legend to Fig. 1, except that ^{32}P-orthophosphate (1 mCi) was used as the radioactive RNA precursor. Mononucleotides resulted from alkaline hydrolysis of the wheat embryo RNA were separated by column and paper chromatography[2]. Base composition of the newly synthesized RNA was calculated from ^{32}P distribution among the isolated nucleotides.

We conclude that the transcriptional events are activated in a cascade manner after the wheat embryo is exposed to optimal germination conditions. Cascade activation requires RNA synthesis to reach some initial level soon after the start of germination and to cease to rise further until the next activation step, after which the synthesis proceeds with greater intensity. Three successive activation steps were recognized and shown to be concerned with the initiation of mRNA, rRNA and tRNA synthesis, in that order. These, and previously reported observations[1,2] on DNA, RNA and protein synthesis in germinating wheat embryos, as well as mitotic index data obtained for the same material (J. Eberhardt, personal communication), are included in a scheme illustrating the sequence of major biosynthetic events triggered at germination (Fig. 2). This sequence is similar to that induced in animal cells in response to the stimulus to proliferate[14–16].

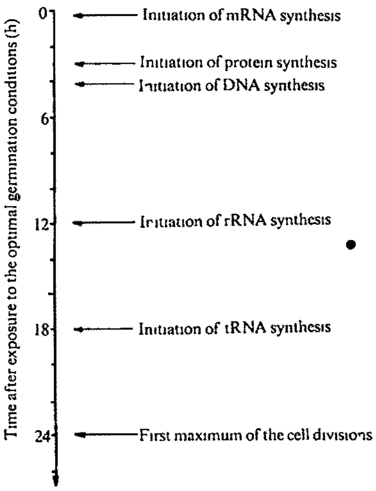
Time after exposure to the optimal germination conditions (h)
0
6
12
18
24
Initiation of mRNA synthesis
Initiation of protein synthesis
Initiation of DNA synthesis
Initiation of rRNA synthesis
Initiation of tRNA synthesis
First maximum of the cell divisions

Fig. 2 The sequence of major biosynthetic events triggered in the wheat embryo during early germination.

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Involvement of a Carbohydrate Group in the Active Site for Surface Guided Reassociation of Animal Cells

THE coordinated cell interactions which occur during development are thought to be due to molecular gradients throughout critical tissue zones[1] or to specific cellular adhesions[2,3] A model system of the latter was described in 1907 by H V Wilson[4,5] who dissociated a yellow and a red species of marine sponge, mixed the cell suspensions and found that the cells sorted into species specific aggregates of the two separate colours Such sorting out occurs also in embryonic vertebrate cells[2] and was found to be organ specific[3] Specific reaggregation and sorting out are assumed to be guided by specific macromolecular components of the cell surface Surface components have been obtained from chick neural retina[6] and mouse cerebrum[7] which preferentially enhance the aggregation of cells from the homologous tissue

The species specific reaggregation of sponge cells observed by Wilson is mediated by a similar factor (aggregation factor, AF) released from the sponge cell surface[8-10] Studies of AF indicate that it is a high molecular weight glycoprotein which requires Ca^{2+} for biological activity[11,12] Preliminary evidence from this laboratory suggested that specific carbohydrates are directly involved as determinants of the specificity of AF from at least one species of sponge[13] We report here further studies into the involvement of carbohydrates in the aggregation-enhancing activity of *Microciona prolifera* AF

The high proportion of carbohydrate present in AF, as well as its sensitivity to periodate (5 mM at 4° C for 12–15 h), suggest that carbohydrates may be involved in AF activity Therefore we tested the ability of the carbohydrates commonly found in glycoproteins to inhibit AF activity (Table 1) Only glucuronic acid was an effective inhibitor and the inhibition was only observed when chemically dissociated cells were pre-incubated with glucuronic acid and then AF was added When the order of addition was reversed inhibition was rarely observed This suggests that glucuronic acid residues present in AF are important for *M prolifera* AF activity The involvement of glucuronic acid in AF action is not a general property of sponge AF, as glucuronic acid had no effect on the aggregation of a second species (*Cliona celata*) by its AF

Uronic acids are known to bind Ca^{2+} and AF requires Ca^{2+} for activity[8] Therefore we tested the possibility that glucuronic acid inhibition of AF is due only to its ability to bind Ca^{2+} We attempted to overcome glucuronic acid inhibition of aggregation by the addition of Ca^{2+} to chemically dissociated cells before the addition of AF Glucuronic acid inhibited aggregation even when a three-fold molar excess of Ca^{2+} was added, while galacturonic acid and glucose had no effect on aggregation even when the latter sugars were present at twice the molar concentration of Ca^{2+} Furthermore, titration experiments (Radiometer, Copenhagen) which easily demonstrated Ca^{2+} binding by EDTA did not indicate Ca^{2+} binding by glucuronic acid at a Ca^{2+} to glucuronic acid ratio of 6 1 and 3 1

Table 2 Effects of Glycosidase Digestion on AF Activity

Enzyme digestion of AF	Degree of aggregation
Control without glycosidase	4+
Glycosidase added	0
Glycosidase+0 1 M glucuronic acid	4+
Glycosidase+0 1 M glucose galacturonic, sialic acid or N-acetylglucosamine	0

Crude *Helix pomatia* enzyme (Endo Labs, Long Island) was diluted to a final concentration of 240 U ml^{-1} with 0 1 M Tris buffer (*p*H 7 7) containing 10 mM CaCl$_2$ The enzyme preparation was incubated for 2 h at room temperature with AF diluted to a final protein concentration of 80 μg ml^{-1} Carbohydrates were added to the glycosidase preparation before the addition of AF The digests were chilled in ice, dialysed overnight in 100 volumes of ice-cold seawater and tested for AF activity The aggregation assay was conducted for 20 min at room temperature in 3 ml total volume of seawater containing approximately 10^7 cells and 2 5 ml of the digest Control experiments indicated that the glycosidase present in the aggregation assay did not cause the aggregation of CMF cells in the absence of AF

Digestion of AF by a non-specific glycosidase preparation from *Helix pomatia* also inhibited AF activity (Table 2) End-product inhibition of a similar non-specific preparation has been used to define the carbohydrate involved in lympho-

Table 1 Inhibition of *M prolifera* AF Activity by Carbohydrates

Carbohydrate	Concentration (mM)	Degree of aggregation	Carbohydrate	Concentration (mM)	Degree of aggregation
None	—	4+	Glucose	50	4+
Cells only, no AF	—	0+	Galactose	50	4+
Glucuronic acid	5	4+	N-Acetylglucosamine	50	4+
Glucuronic acid	25	2+	N-Acetylgalactosamine	50	4+
Glucuronic acid	100	1+	α-Methyl-glucose	50	4+
Cellobiuronic acid	5	2+	α-Methyl-mannose	50	4+
Cellobiose	50	4+	Mannose	50	4+
Galacturonic acid	50	4+	Fucose	50	4+

Chemically dissociated cells and AF were prepared by the methods developed by Humphreys[8] All AF preparations were 105,000*g* pellets resuspended in complete artificial seawater[17] Chemical analyses indicated hexose to protein ratios of 51 49, in good agreement with earlier reports of sugar to protein ratios for *Microciona* AF of 1 1 (ref 12) In addition, we found that 15% of the hexose consisted of uronic acids The carbohydrates indicated were preincubated for 5 min at room temperature in a 25 ml Erlenmeyer flask containing 2–5 × 10^7 cells in 2 ml of seawater 1 ml of seawater containing AF preparation (30 μg ml^{-1} protein) was then added and the degree of aggregation scored after 20 min of rotation at room temperature (36 r p m , 4 cm diameter circle) Aggregation was determined according to the following scale 4+ = one to five clumps, 3+ = five to 100 clumps, 2+ = 100–5,000 clumps, 1+ = fine granulation and distinguishable from 0, 0 = no visible granulation

Concentrations of carbohydrates given are the final concentrations during incubations Uronic acids and derivatives were buffered to *p*H 7 0 with NaOH

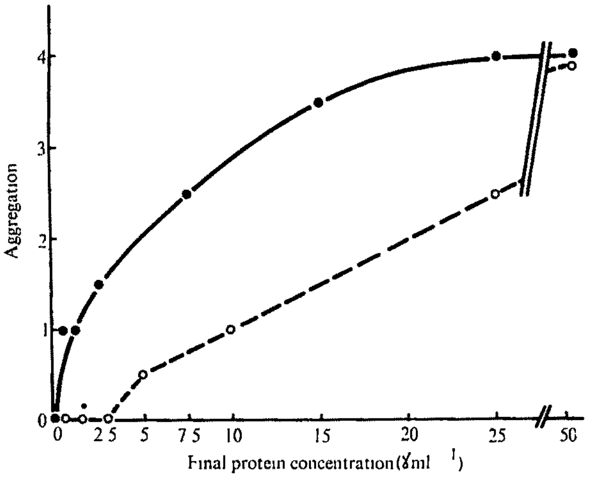

Fig. 1 Aggregation of *M. prolifera* cells by *M. prolifera* AF (●) and by *Haliclona occulata* AF (○). The original protein concentration of the *Microciona* factor preparation was 750 μg ml^{-1} and the *Haliclona* factor preparation contained 150 μg ml^{-1} of protein, which means that adding 0.10 ml of each factor brings the final protein concentration to 5 μg ml^{-1} in the case of *Haliclona* factor and 25 μg ml^{-1} in the case of *Microciona* factor. The degree of aggregation indicated was attained in 20 min at 22° C, aggregation did not occur in the absence of factor, and there was no significant increase in aggregation during the subsequent 60 min. The greater efficiency of *Microciona* factor relative to that of *Haliclona* factor for *Microciona* aggregation was observed when readings were taken before 20 min. Instead of the two-fold higher specific activity (based on protein concentration of the factor preparations) a 3–5-fold better efficiency was observed for the homotypic (*Microciona* factor and *Microciona* cells) against the heterotypic (*Haliclona* factor and *Microciona* cells) combination of factor and cells.

cyte homing[14]. End-product inhibition of the *Helix* enzyme by glucuronic acid, but not glucose or galacturonic acid, during treatment of AF with the non-specific enzyme protected AF from digestion by the glycosidase preparation. The effect of *Helix pomatia* glycosidases on AF activity is thus probably due to the removal of glucuronic acid from AF. These experiments lead us to conclude that *Microciona* AF contains glucuronic acid residues which are directly involved in mediating the reaggregation of *Microciona* cells.

Direct proof of this conclusion demands isolation and complete chemical analysis of AF fragments which inhibit AF activity. We have begun such experiments and preliminary studies lead to some specific low molecular fragments isolated on a 'Sephadex' column from a pronase digest which were strong inhibitors and have a very high carbohydrate to protein ratio.

The reaggregation of *Microciona* cells has been reported to occur in a species specific fashion[8]. As a preliminary experiment to investigations on the specificity of *Microciona* AF, we tested the ability of *Microciona* AF and *Haliclona occulata* AF to aggregate *Microciona* cells. We observed (Fig. 1) that both AF preparations were able to mediate aggregation, although the *Haliclona* AF was only 10% as effective as *Microciona* AF on a volume basis and less than 50% as efficient when the comparison is based on protein content. This preliminary observation suggests that species specific reaggregation is based on quantitative, as well as qualitative, differences between the surface properties of these two species of sponge. The apparent contradiction in reports (for example ref. 16) that mechanically dissociated cells show species specific reaggregation, but that AF preparations from the same species are not specific, may, in some cases, be resolved by experiments (such as described in Fig. 1) which investigate the qualitative and quantitative aspects of the interaction of chemically dissociated cells with AF from both the homologous and heterologous species.

Previous studies on sponge cell aggregation have indicated that aggregation factor is inactivated by periodate oxidation[11] as well as by protease treatment[11]. We have here proved that carbohydrates can provide specificity to the action of AF. Although inactivation by proteolytic enzymes seems to argue against carbohydrates as the source of specificity, the model in ref. 15 explains such observations as it suggests that the protein is the structural carrier of the carbohydrate groups involved in specificity (Fig. 1, ref. 16). This working model is being used as a guide for our future research and will be revised as more evidence is obtained concerning the mechanism of aggregation factor mediated sponge cell reaggregation.

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Two Component System for Surface Guided Reassociation of Animal Cells

SPONGE cells dissociated by means of seawater containing no calcium or magnesium release a large molecular factor (AF) which is required for specific reaggregation at 4° C into multicellular agglomerations the size of small sponges[1]. The function of the aggregation factor (AF) in *Microciona prolifera* is dependent on a specific carbohydrate[2]. Here we describe the isolation of a second macromolecular component, other than AF, which is necessary for reaggregation, and which seems to remain on the surface of the cell after removal of the aggregation factor, and to interact with intercellular AF. Until its function is clearly understood, we shall describe it as a baseplate.

Earlier we found that hypotonic treatment of cells can release components from the surface of tumour cells[3] Chemically dissociated (2×10^8) *M prolifera* cells treated with 0 09-0 07 M NaCl at 37° C for 30 min completely lost the ability to aggregate in the presence of AF (Table 1, experiments 7 and 4) The medium from the hypotonic shock treatment contained a heat labile, pronase sensitive, non-dialysable component that could not be pelleted at 105,000*g* or extracted as a lipid[4] and which was capable of inducing aggregation in shocked cells if added simultaneously with AF and calcium (Table 1, experiments 6–9) Hypertonic shock (3 M NaCl) did not lead to the removal of such a component If this component has acceptor function for the AF, that is if it acts as a baseplate, it should bind to cells which lack it and only then should such cells be responsive to AF Addition of the baseplate fraction to hypotonically treated cells, even in the absence of calcium or AF, and subsequent removal of the incubation medium and addition of AF led to aggregation Reversing the order of incubation with AF and baseplate did not result in aggregation Simultaneous addition of preincubated AF and baseplate fractions also restored aggregation (Table 1, experiment 9)

Table 1 Whole Cell Aggregation Studies using *M prolifera*

Experiment No	Cell type used	AF added	Baseplate added	Glu-COOH added	Degree of aggregation
1	Mech	–	–	–	4+
2	Mech	+	–	–	4+
3	CMF	–	–	–	–
4	CMF	+	–	–	4+
5	CMF	–	+	–	–
6	CMF+Hy	–	–	–	–
7	CMF+Hy	+	–	–	–
8	CMF+Hy	–	+	–	–
9	CMF+Hy	Preincubated		–	3+
10	CMF+Hy	Second	First *	–	3+
11	CMF+Hy	First *	Second	–	–
12	CMF	Preincubated		–	–
13	CMF	Second	First †	–	–
14	CMF	First †	Second	–	4+
15	Mech	–	+	–	2+
16	CMF+Hy	Second	Preincubated		–
17	CMF	Second	Preincubated		4+
18	CMF	Second	–	First †	–
19	CMF	–	–	+	4+
20	Mech	–	–	+	–

The incubation mixture included 0 05 ml AF[2], 0 3 ml baseplate (about 700 µg protein ml^{-1}), 5×10^{-2} M glucuronic acid (Glu-COOH) final concentration, and seawater to bring the volume to 2 0 ml The reaction was started by addition of 1 0 ml of sponge cell suspension (5×10^7 cells ml^{-1}) CMF, chemically dissociated[2], Mech, mechanically dissociated, CMF+Hy, chemically dissociated, then hypotonically shocked cells Readings were taken at 15 min after initiation of shaking at room temperature Scorings were as in the previous report[2]

* Added to cells either in calcium-magnesium free seawater or in calcium-magnesium free seawater to which 2×10^{-3} M Ca^{2+} was added Cells were then spun for 90 s at 1,000 r p m , re-suspended in calcium-magnesium free seawater and the second reagent added

† First reagent was in contact with cells for 5 min, only then was the reaction started with second reagent

Further evidence for a direct interaction between AF and baseplate activity came from the following experiment The baseplate preparation was capable of inactivating AF, presumably by binding to it, if the two were preincubated and then added to unshocked, chemically dissociated cells which still carried their baseplate (Table 1, experiment 12) The order of addition, however, was again important (Table 1, experiments 13 and 14)

Further support for the concept that baseplate material binds to AF comes from another inhibition experiment Mechanically disrupted cells still carry enough AF on their surface to aggregate in seawater containing calcium Baseplate material should bind to the AF on such cells and inhibit aggregation as can indeed be seen in experiment 15 of Table 1, if compared with experiment 1

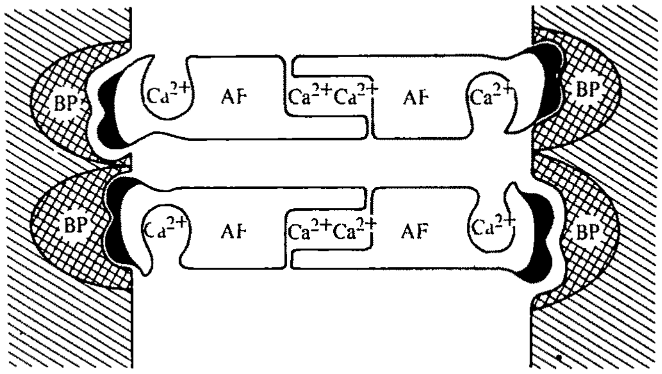

Fig 1 Tentative model for specific cell–cell interactions in tissue construction Two macromolecular AFs are illustrated each consisting of at least two subunits The black termini at each pole carry the carbohydrates, which are recognized by the baseplate (BP) anchored in adjoining cell surfaces

The apparent role of glucuronic acid is as a recognition site on AF, necessary for AF baseline binding, as described in the previous paper[2] This suggestion is strengthened by the fact that the baseplate fraction is rendered non-functional if preincubated with glucuronic acid, both for direct activity measurements with cells lacking both AF and baseplate (Table 1, experiments 16 and 10) as well as for inhibitory experiments with cells lacking only AF (Table 1, experiments 17 and 13) Further support comes from experiments 18 and 19 in which glucuronic acid inhibited aggregation of cells in the absence of AF but still containing baseplate, if it was preincubated with, and capable of binding to, the baseplate before AF was added and not if added together with AF

In an effort to obtain a cell-free test system either AF or an AF free baseplate fraction was covalently attached to 'Sepharose' beads[5] When AF coated beads were added to a suspension of chemically dissociated cells, the cells bound to the beads If AF beads were added to hypotonically shocked, chemically dissociated cells, the cells had no affinity for the beads Similarly, baseplate beads bound only shocked cells but not chemically dissociated cells Such results suggest that the beads might be used as an acellular aggregation system

The results of aggregation experiments with coated beads are shown in Table 2 It is clear that AF beads act similarly to mechanically dissociated cells (Table 2, experiments A–C, and Table 1, experiments 1, 2, 15 and 20), with the exception that glucuronic acid inhibits aggregation of mechanically dissociated cells but does not affect AF beads This is to be expected because AF beads bind only by factor factor interaction, while the mechanically disrupted cells (where some of the disruptions have occurred between AF and baseplate) interact primarily by factor baseplate binding (see model below) It also seems that beads coated with baseplate act similarly to chemically dissociated cells (Table 2, experiments D–I, and Table 1, experiments 3–5, 12, 18, 19)

In an effort to use AF beads to purify baseplate activity by affinity chromatography we found in preliminary experiments that all baseplate-like activity was bound to an AF bead column and none to an unsubstituted column of activated beads Figure 1 summarizes our observations from this and the previous paper in a tentative model The salient points are the following (1) Aggregation requires two different components, an intercellular aggregation factor (AF) and a baseplate (BP) anchored within the cell surface (2) The AF is a multicomponent and multivalent macromolecular complex of carbohydrates and protein One unit contains among other components at least two, probably several, identical subunits involved in the recognition process (3) In the sponge cell interaction examined, carbohydrate on the AF seems to be recognized as an antigen by a surface protein serving as an antibody-like baseplate for the AF In calcium–magnesium free seawater removal of small amounts of calcium will loosen up peripheral attachment points of the AF and lead to its release Prolonged incubation in calcium–magnesium free seawater or incubation in EDTA will eventually remove tightly bound calcium and inactivate AF Mechanical dissociation of cells randomly disrupts AF-baseplate interactions on two adjoining cell surfaces Among many possibilities this might be due to a certain asymmetry in anchorage of the AF as illustrated symbolically by different gap widths between the carbohydrate end of AF and the baseplate

Table 2 Bead Aggregation Studies using 'Sepharose 4B Beads to which *M prolifera* AF or Baseplate (BP) has been Covalently Linked[6]

Experiment No	Beads added containing	AF added	Baseplate added	Glu-COOH added	Degree of aggregation
A	AF	–	–	–	3+
B	AF	–	+	–	–
C	AF	–	–	+	3+
D	BP	–	–	–	–
E	BP	+	–	–	4+
F	BP	–	+	–	–
G	BP	Preincubated		–	–
H	BP	Second	–	First*	–
I	BP	First*	–	Second	4+
J	AF+BP	–	–	–	4+

The reaction mixture is the same as in Table 1 except 0 05 ml bead suspension in calcium–magnesium free seawater replaces 1 0 ml of sponge cell suspension Aggregation of the beads was almost immediate after addition of calcium-containing seawater (10 s to 2 min) The extent of aggregation was scored on the following scale 4+ showed 90% of the beads in a single clump, 3+ 90% of the beads as two to ten clumps, 2+ showed 90% of the beads as eleven to 200 clumps, 1+ showed 90% of the beads as microscopic clumps each of more than five beads

* First reagent was in contact with beads for 2 min Only then was the second added and the degree of aggregation measured 2 min after the second addition

We should like to advocate the use of beads covered with cell specific surface components as model systems for the study of some embryological cell–cell interactions Whether such studies will be applicable to organogenesis in general and to other specific morphogenetic interactions in mammalian cells during differentiation is not yet clear Our semi-quantitative studies will now have to be put on solid quantitative and biochemical grounds and the species specificity of both AF and baseplate activity will have to be investigated

A preliminary note of part of this work was published previously[6] Since then Dr T Humphreys has informed us that he has isolated a component similar to the baseplate material by another technique

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Recognition of Protein Structure in Leukocyte Chemotaxis

RECOGNITION of antigen in the specific immune response is well understood Recognition of foreign or altered self material by the cells which mediate non-specific immunity has received little attention In tissue injury or bacterial infections, many proteins may become enzymatically degraded or conformationally altered Here I report a study of the chemotactic migration of neutrophil leukocytes towards the model proteins, haemoglobin and myoglobin, in their native and haem-free conformationally altered forms, and show that conformational changes in these proteins are recognized by leukocytes and evoke a chemotactic response, although the native proteins are inactive A model for the molecular basis of this recognition is proposed

Haemoglobin was prepared from normal adult human red cells by the method of Rossi-Fanelli *et al*[1] and myoglobin (horse heart) and haemin were purchased from B D H Ltd, Poole, Dorset Neutrophil leukocytes were obtained from the leukocyte-rich plasma after dextran sedimentation of heparinized normal human blood Monocytes were separated from these on 'Ficoll-triosil' The chemotactic technique used was as previously described[2] Migration was quantified by measuring the distance migrated through a micropore filter in a fixed time by the leading front of cells[3] Globin (apohaemoglobin or apomyoglobin) was prepared from haemoglobin and from myoglobin by the cold acid-acetone method of Rossi-Fanelli *et al*[4] Haemoglobin or myoglobin was reconstituted from apohaemoglobin or apomyoglobin by addition of haemin as described previously[5] The formation of globin and the reformation of haemoglobin or myoglobin were measured by changes in the absorption intensity of the spectrophotometric peak in the Soret region (406 nm for haemoglobin 409 nm for myoglobin)

Table 1 Chemotactic Migration of Human Neutrophils towards Various Preparations of Human Haemoglobin and Horse Myoglobin

Sample at 1 mg per ml and *p*H 7 2	Neutrophil migration (μm) in 75 min in 3 μm pore size filters
Oxyhaemoglobin	31
CO haemoglobin	38
Reduced haemoglobin ($Na_2S_2O_4$)	28
Ferrihaemoglobin	37
Apohaemoglobin	93
Myoglobin (Fe^{III})	30
Apomyoglobin	76
Gey's solution (suspending medium for all tests, negative control)	22
Casein 5 mg ml^{-1} (positive control)	105

Table 1 shows that the conformational changes in haemoglobin associated with binding of ligands, such as O_2 or CO or with the change from the ferrous to the ferric state, did not make the protein significantly chemotactic, but when haem was removed from haemoglobin or myoglobin, the resulting globin solutions were chemotactic for human blood neutrophils and monocytes (data not shown) A drop in helical content of from 65% to 52% α helix for haemoglobin[5], and a similar drop for myoglobin[6,7] took place on removal of haem. As it was possible that the acquisition of chemotactic activity on the formation of globin was due to recognition by leukocytes of this loss of folded structure in the protein, and as the unfolding which accompanies the formation of globin can be completely reversed by readdition of haemin to globin to form a haem protein structurally identical to the original native form[5–7], experiments were performed to see whether this refolding was accompanied by loss of chemotactic activity. This proved to be so. Figure 1 shows that the chemotactic activity of apohaemoglobin is progressively reduced as increasing amounts of haemin are added to the protein. At a ratio of one mol of bound haemin per mol of globin dimer, a ratio at which the native form is fully recovered[5], the chemotactic activity is essentially that of the original haemoglobin. Similar results were obtained on addition of haemin to apomyoglobin. The reversible chemotactic activity of haem proteins is, therefore, probably due to recognition of leukocytes of reversible conformational changes in the protein molecule.

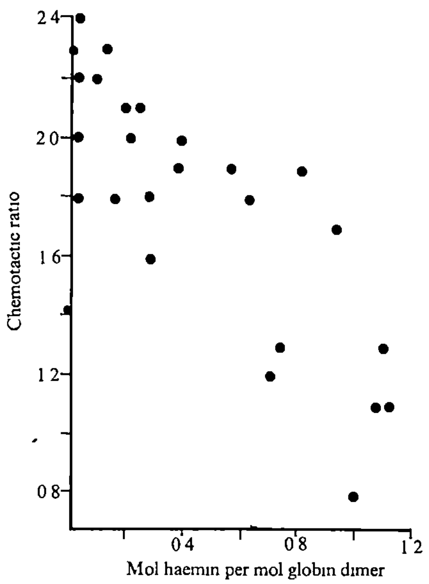

Fig. 1 The chemotactic activity for human neutrophils of apohaemoglobin combined with haemin at varying molar ratios. The chemotactic ratio was taken as the migration (µm per 75 min) towards test sample against the migration towards native ferrihaemoglobin. Note that as the molar ratio of bound haemin is increased, the chemotactic activity of the protein decreases.

In previously reported experiments[2], it was shown that when a protein such as human serum albumin (HSA) was conjugated to various synthetic side groups, non-polar groups, such as tosyl, propionyl or butyryl groups, made the protein more chemotactic for neutrophils than did polar side groups. It was suggested that the chemotactic activity of those conjugated proteins was due to recognition by the leukocyte of externally positioned non-polar groups on a protein molecule. Those experiments also showed that this recognition was unlikely to result from the presence on the leukocyte of a stereospecific receptor for chemotactic factors, as migration of leukocytes towards a protein conjugated to a given side group was not inhibited by the presence of the conjugated substance in excess in free solution. It is likely that the same recognition mechanism may serve for chemotaxis towards denatured proteins as, in native haemoglobin and myoglobin, the non-polar residues are packed into the interior of the molecule but are forced to the exterior when haem is removed. Experiments with HSA[8] have indicated that polymerization of denatured proteins is not necessary for chemotactic recognition but that leukocytes migrate towards denatured proteins in their monomeric form. Therefore, these cells detect conformational changes in proteins without a requirement for stereospecific binding by a receptor. The presence of external non-polar groups on proteins in the environment of the leukocyte might provide a suitable marker leading to a cellular response which results in removal of the damaged protein.

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Tetraploid Mouse Embryos produced by Cytochalasin B during Cleavage

IT has been reported that cytochalasin B can prevent cytokinesis without influencing nuclear division[1]. Cells undergoing mitosis in the presence of cytochalasin B become binucleate and occasionally, with prolonged incubation, multinucleate[1–3]. Treated cells generally resume cleavage upon removal from cytochalasin and reculturing. It has been shown that many of the binucleate cells produced in a BHK21 cell line will develop as tetraploids upon reculturing in fresh medium[4,5]. Here I report the treatment of cleaving mouse eggs with cytochalasin and the establishment of tetraploidy in mouse embryos.

Randomly bred Q strain mice kept under a natural diurnal light cycle were used throughout. Cleaving embryos were flushed from the oviducts of pregnant females 38–40 h *post coitum*. Most of these embryos are two-cell but a few three or four-cell embryos indicated that the second cleavage was imminent. It was therefore possible to allocate each cell to one of the following categories: (1) late G_2 or prophase (nucleus present), (2) division, either metaphase or anaphase (nucleus absent), (3) early G_1/S, with the cell dividing or divided. Although controversy exists as to the first appearance of the G_1 period in the mouse[6] it is doubtful whether one exists at the four-cell stage[7], even in slow-dividing strains[8].

Groups of ten embryos were cultured in 0.1-ml drops of Whitten's medium[9] under mineral oil in 60-mm plastic dishes. They were kept at 37° C and gassed with 10% CO_2 in air. Cytochalasin B (Imperial Chemicals Ltd) dissolved in dimethyl sulphoxide (1 mg ml^{-1}) was added to this medium to give a concentration of 10 µg ml^{-1}. Tests had shown this to be the lowest concentration which would ensure complete inhibition of cytokinesis. Controls, grown with an equivalent amount of DMSO were run concurrently.

Embryos were put into cytochalasin for various periods of time. Many of the cells in G_2/prophase immediately show

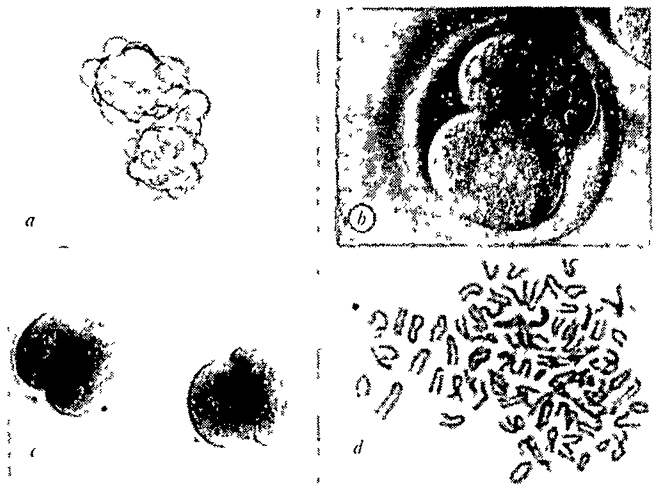

Fig. 1 *a*, A late G_2 two-cell embryo (with zona pellucida removed for clarity of illustration) showing extensive blistering of its cell surface after 7 min in 10 µg ml^{-1} cytochalasin B. *b*, A two-cell embryo with one blastomere binucleate and one with its nucleus in division after several hours in 10 µg ml^{-1} cytochalasin B. *c*, Two embryos recultured after becoming binucleate. One blastomere is still binucleate, one has a large metaphase plate (contributed to by two nuclei) and two blastomeres have already divided. These embryos were fixed with 3% glutaraldehyde before photography. *d*, A metaphase plate from the 12.5-d-old tetraploid embryo.

a vigorous cell membrane blistering (Fig. 1*a*). The blisters appear within 5 min and persist for some 10–15 min before the cell regains its normal smooth surface and shape. Some nucleated two-cell blastomeres do not blister and these have been found to be earlier in the G_2 phase than cells which do blister. These cells remain smooth and even when they approach and undergo mitosis show no indication of blisters.

Most cells in division remain smooth, exceptionally some late anaphase or telophase cells blister for about 10 min. Any cleavage furrow present recedes rapidly and disappears. Cleavage furrows fail to develop in cells which have not started cytokinesis. These observations are similar to those made on cleaving *Xenopus* and *Arbacia* eggs[10,11] except that in those embryos the initiation of cleavage furrows is not prevented.

Cells in G_1/S show vigorous blistering (lasting 10–15 min) then revert to smooth surfaced cells. Cells at least 1 h into G_1/S do not blister but remain smooth and apparently unaffected by cytochalasin.

In those cells that are prevented from dividing by cytochalasin, the nuclei divide normally, at the correct time, giving rise to binucleate cells. The daughter nuclei then migrate to opposite poles of the cell where they come to lie very close to the cell surface (Fig. 1*b*). This process takes 2–4 h. Although there are reports of spontaneous enucleation of cells as a result of cytochalasin treatment[1,12,13] this has never been observed in these mouse embryos.

Upon removal from cytochalasin and culture in fresh medium the binucleate cells behave differently depending upon their position in the cell cycle. If the nuclei are close together (corresponding to early G_1/S) when the cell is recultured, violent cell membrane blistering (lasting 10–15 min) occurs followed by the formation of several cleavage furrows. These furrows divide the cell into several pieces, two of which contain nuclei. These nucleated pieces will continue to develop normally, and form small but otherwise normal diploid blastocysts.

If the nuclei are at the poles of the cell when it is removed from cytochalasin then the cells remain in this condition until the next cleavage, which is a few hours delayed. Then, in about 60% of embryos, the nuclei move back into the cell centre and contribute to a single spindle (Fig. 1*c*). The cells divide, giving rise to a tetraploid four-cell embryo which will continue to cleave and form a tetraploid blastocyst. These blastocysts contain a considerably reduced cell number (control, thirteen blastocysts, mean cell no. 49.9±2.8, cytochalasin, sixty blastocysts, mean cell no. 19.1±0.67). By selection of smooth surfaced two-cell embryos a few hours after removal from cytochalasin, which avoids those embryos which reverted to diploid and those where asynchrony has produced a diploid/tetraploid mosaic, it is possible to collect blastocysts which are uniformly tetraploid.

Some embryos fail to recover the ability to cleave after removal from cytochalasin although their nuclei continue dividing, each time contributing to a common spindle, and the cells become highly polyploid. In some twenty or thirty of these embryos I have encountered two two-cell "blastocysts" which were sixteen-ploid and a number of octaploid embryos.

From these observations a routine procedure was established for the production of tetraploid embryos, as follows. Two-cell embryos were put into cytochalasin between 1700 h and 1800 h on the second day of pregnancy and removed at 0600 h the following day. After this period no cell reverts to the diploid condition but 10–15% fail to cleave again. About 20–25% are somewhat delayed in their next cleavage. Usually about 40% of the initial two-cell embryos produce blastocysts but yields as high as 75% are possible.

Tetraploid blastocysts were transferred to the uteri of pseudopregnant foster mothers. Autopsies of the twenty-four recipient females examined so far showed that fourteen were pregnant and contained seventy-eight implantations from 112 blastocysts transferred. The majority of these implants (sixty-seven) showed that embryonic development was extremely limited and did not proceed into organogenesis (beyond 8.5 d). In similar experiments, Tarkowski and Witkowska (personal communication) have found that in tetraploid egg cylinders the formation of foetal membranes proceeds normally but the embryo itself does not develop. This syndrome is similar to that described for triploid mouse embryos[14].

The remaining embryos in my experiments have shown development beyond the egg cylinder stage. Chromosome analysis has shown all to be tetraploid (Fig. 1*d*). Ten showed normal development up to the time of autopsy (including three live at term). The other, autopsied at 17.5 d, was abnormal. The ventral body wall of the embryo had failed to close and the viscera were externalized. The embryo was alive and showed no other gross abnormalities. This represents considerably greater development of tetraploids than has been achieved after cell fusion[15] or other treatments[16] in mammals.

Histological examination of several target sites in a 12.5-d tetraploid, compared with a similar stage diploid, indicates that the tetraploid is of normal dimensions but composed of fewer, larger cells. This suggests that the cell cycle time is not altered to any great extent by tetraploidy, at least up to 12.5 d of gestation.

It would seem from the results so far that there are not necessarily any developmental problems inherent in being tetraploid although death soon after implantation may sometimes be due to genetic imbalance (for example, aneuploidy, anomalies of X chromosome or sub-chromosomal inactivation). It is likely that the very low cell number in tetraploid blastocysts plays a significant part in reducing the developmental potential of the embryo[17,18]. The technique of embryo aggregation[19,20] is being used to investigate this parameter.

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Natural and Synthetic Sources of Circulating 25-Hydroxyvitamin D in Man

THE antirickettic sterols are both assimilated from the diet and endogenously produced by ultraviolet irradiation of cutaneous 7-dehydrocholesterol[1-3] Before the modern practice of supplementing foods with irradiated ergosterol (ergocalciferol, vitamin D_2), deficiency states were frequently observed in subjects whose dark skin colour and/or minimal exposure to sunlight minimized the natural endogenous production of cholecalciferol (vitamin D_3)[4] It has been generally accepted that casual exposure to sunlight and average diets provide enough antirickettic sterol to prevent osteomalacia in the adult (American Academy of Pediatrics 1963) Infants, however, are recognized to require vitamin D supplementation, for their maternally derived stores wane at a time when their natural foods are a poor source and their exposure to ultraviolet radiation unreliable Supplementation of foods with vitamin D_2 has thus become a widespread and successful practice which has subsequently undergone quantitative revisions in several countries

The minimum adult dietary requirement of vitamin D has been estimated to be 75 IU d^{-1} in England[5] Previous bioassay studies of human sera revealed increased antirickettic potency in subjects exposed to sunshine for most of the year[6], and in persons fed large amounts of the synthetic vitamin D_2 (ref 7) Precise quantification of the cutaneous contribution to body vitamin D stores has not been feasible to date but it has been observed that human exposure to ultraviolet radiation is followed by enhanced intestinal absorption of calcium[8] and healing of vitamin D-deficiency states[9] It is now recognized that vitamin D undergoes 25-hydroxylation in the liver[10] The products, 25-hydroxyvitamins D_2 and D_3, are both known to be 150% more potent than the parent vitamin by bioassay[11,12] Subsequent 1-hydroxylation in the kidney produces an even more potent metabolite of the vitamin[13] but the chief circulating form of the vitamin in man has been identified as the 25-hydroxy derivative[14] Previous rat bioassay analyses of whole serum or serum extracts for antirickettic activity have, therefore, been nonspecific because the assay animals are capable of responding equally to vitamin D_2 or D_3, as well as to their 25-hydroxy and 1,25-dihydroxy derivatives

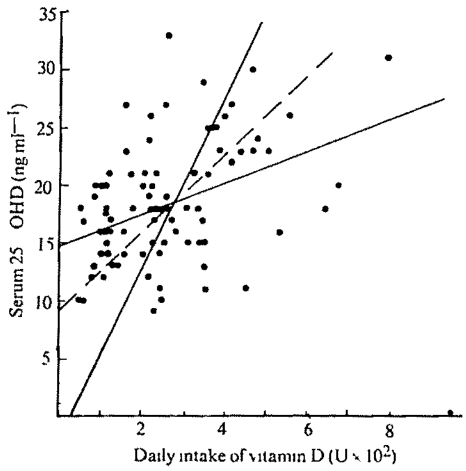

Fig 1 Total serum 25-OHD concentations as a function of estimated daily vitamin D ingestion by eighty-four Caucasian adults residing in St Louis, Missouri ——, Regression on each variable, - - -, the "reduced major axis" $r=0\ 42$, $P<0\ 001$

While applying a radioligand assay for 25-hydroxyvitamin D (25-OHD)[15] to human sera obtained randomly during the calendar year, we obtained diet histories quantifying average weekly vitamin D ingestion and estimates of time spent outdoors from eighty-four Caucasian adults (age range 16 to 70 yr) who had no evidence of disease or recent drug use Their circulating 25-OHD levels, as a function of daily vitamin D ingestion, are shown in Fig 1 The mean 25-OHD concentration for the group was $18\ 6\pm5\ 2$ (s d) ng ml^{-1}, and a significant ($P<0\ 001$) correlation between serum 25-OHD concentration and vitamin D intake was found An ordinate intercept of 14 7 ng ml^{-1} was observed The "inverse" regression line and the "reduced major axis" are also shown[16] The 95% limits of the intermediate intercept are −8 83 and 26 89 ng ml^{-1} with a mean of 9 03 ng ml^{-1} Thus, although the correlation between the two variables is significant, much of the variation in serum 25-OHD can be accounted for by factors other than vitamin intake Also, the paucity of low intake values and data scatter prevented evaluation of a possible curvilinear relationship in which proportionately more of a smaller amount of the vitamin undergoes hydroxylation[17] Plotting 25-OHD concentration against hours outdoors (<20 h per week in all cases) yielded a scattergram with no definite correlation The estimates of time spent outdoors, however, were vague and often given in ranges, and were not indicative of other obvious variables such as clothing and weather Our diet surveys indicated that some of the ingested vitamin D was in the form of D_3 but that the dominant source was the D_2 added to milk, cereals and multivitamin capsules

We have previously shown that the radioligand assay cannot distinguish between 25-hydroxyergocalciferol (25-OHD$_2$) and 25-hydroxycholecalciferol (25-OHD$_3$)[18] In order to examine directly whether or not the dominant circulating moiety of 25-OHD was indeed 25-OHD$_3$, we had to achieve chromatographic separation of 25-OHD$_2$ from 25-OHD$_3$ In this way we could establish whether the correlation observed in Fig 1 reflected the partial influence of vitamin D_2 derived from diet on circulating 25-OHD During the purification of ^{3}H-25-OHD$_2$ produced by rickettic rats *in vivo*[1], we observed that the gradient silicic acid column[19] fraction of ^{3}H-25-OHD$_2$ eluted before ^{3}H-25-OHD$_3$ on a standard calibrated LH-20 'Sephadex' column (65 35 chloroform/hexane)[20]. ^{3}H-Ergocalciferol, 1,200 d p m per IU was administered to rickettic rats intraperitoneally, and blood was obtained 24 h later By changing the solvent mix-

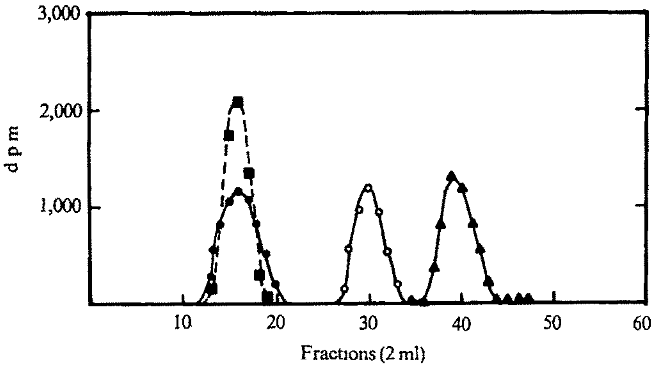

Fig. 2 Chromatographic profiles of radioactive ergocalciferol (D_2), cholecalciferol (D_3), 25-hydroxyergocalciferol (25-OHD_2) and 25-hydroxycholecalciferol (25-OHD_3) separately run on a calibrated 1 × 60 cm column of LH-20 'Sephadex' slurried in 50 50 chloroform/*n*-hexane ▲, 25-OHD_3, ○, 25-OHD_2, ■, D_3, ●, D_2

ture to 50 50 and decreasing the volume of the collection fractions to 2 ml, the 25-hydroxy derivatives of vitamin D_2 and vitamin D_3 were separated (Fig 2) As shown, the parent vitamins were not separated in this system High specific activity ^{3}H-(26,27)25-OHD_3 (19 7 Ci mmol^{-1}, Radiochemical Centre, Amersham) was used as a marker for the isolation of 25-OHD_3 from serum extracts by column chromatography

Six normal adults were sampled between January and July, and the sera extracted as described previously[21] Separate aliquots were subjected to the usual stepwise silicic acid column elutions[15] or to chromatography on a 1 0 × 60 cm column of LH-20 'Sephadex' equilibrated in equal parts of chloroform and *n*-hexane Recoveries were monitored by determining recovery of added radioactivity (tracer ^{3}H-25-OHD_3) in the fractions obtained from the silicic acid and LH-20 'Sephadex' columns Aliquots of the total 25-OHD (both 25-OHD_2 and 25-OHD_3) from silicic acid columns were measured in the radioligand assay In the same assays, aliquots from those fractions of the LH-20 'Sephadex' columns marked by tracer 25-OHD_3 were also monitored Thus, total 25-OHD and 25-OHD_3 concentrations were determined by assaying the silicic acid stepwise elution and LH-20 'Sephadex' fractions respectively

As indicated in Table 1, most of the circulating 25-OHD in the sera from all six normal subjects was 25-OHD_3 Estimated dietary intakes of vitamin D were 150 to 350 U d^{-1} and there was no history of inordinate sunlight or ultraviolet exposure in any of the subjects Serum 25-OHD_3 averaged 84% of total serum 25-OHD content in this small group, supporting the influence of non-ingested sources indicated in the larger population survey (Fig 1) Blood was obtained from two of the female subjects in late July, following several weeks of 25 to 35 h per week of sunbathing. As shown, the increases in total serum 25-OHD could be directly attributed to the increases in the 25-OHD_3 fractions (Table 1) A hypoparathyroid subject who had taken 50,000 U of vitamin D_2 per day for 6 yr was studied 4 months after the vitamin therapy had been discontinued Analysis of this serum extract revealed only 18% (11 ng ml^{-1}) of the total 25-OHD to be 25-OHD_3, consistent with previous chronic ingestion of large amounts of D_2 Also shown is the fractionation of serum 25-OHD observed in a young black male, one week after a subcutaneous injection of 3 mg each of vitamin D_2 and vitamin D_3 Before therapy he had taken anticonvulsant drugs for many years and presented with hypocalcaemia and a total serum 25-OHD concentration of 0 3 ng ml^{-1} The similar amounts of 25-OHD_2 and 25-OHD_3 in his serum 1 week after administration of D_2 and D_3 suggest comparable hepatic 25-hydroxylation of each form of the vitamin in this subject

Table 1 Total Serum 25-OHD and 25-OHD_3 Concentrations in Various Subjects

Subjects	Race/sex	Month serum obtained	Total serum 25-OHD (ng ml^{-1})	% of total serum 25-OHD as 25-OHD_3
Normal				
O H	C/M	February	16	90
R W	C/M	February	13	71
S B	C/M	February	24	91
M M	C/F	January	24	91
M T	C/F	January	21	83
M T	C/F	July	33	88
J U	C/F	January	25	82
J U	C/F	July	41	90
Hypoparathyroid				
E M	C/F	October	62	18
(50,000 IU vitamin D_2 d^{-1} stopped 4 months previously)				
Anticonvulsant Rx				
C W	B/M	September	12	46
120,000 IU D_2 and 120,000 IU D_3 given 7 d before				

Our observations demonstrate that 25-OHD_3 is the dominant circulating moiety of 25-OHD in St Louis Caucasian adults and also indicate that ingestion and endogenous production of vitamin D_3 is the principal source of the vitamin in the population Unless the diet is unusually rich in fish products, however, there are no important ingested sources of vitamin D_3 (ref 22) Therefore, circulating 25-OHD_3 levels seem to reflect primarily endogenous D_3 production by the skin Our results thus apparently represent the first direct quantification of the separate contributions of cutaneous production of D_3 and dietary ingestion of D_2 in man

These conclusions, based on plasma levels of 25-OHD_2 and 25-OHD_3 carry the implicit assumption that D_2 and D_3 are metabolized in an identical manner[11 12]. Vitamin D_2 and vitamin D_3 are generally considered equipotent in man but direct comparative examinations of their metabolism have not been performed Although it is known that vitamin D_3 is stored in various tissues[23,24], factors affecting its assimilation, transport and release from storage sites are not well defined Even less is known about the metabolic fate of D_2 The dual application of radioligand assay and chromatographic techniques described here could be a most useful method for distinguishing synthetic and natural vitamin D sources and separately assessing their metabolic disposition

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First Record of the Palaeocene Primate *Chiromyoides* from North America

PALAEOCENE fossil primates are known only from the European and North American continents. Fourteen genera and numerous species from North America have been described[1,2], and four genera (*Plesiadapis*, *Chiromyoides*, *Berruvius*, *Saxonella*) are recorded from Europe[3]. Only one primate genus, *Plesiadapis*, was previously known from the Palaeocene of both continents; the new species of *Chiromyoides* described below extends the range of this genus to North America. Addition of *Chiromyoides* brings to seven the number of mammalian genera known from the Palaeocene of both Europe and North America.

Stehlin[4] gave the name *Chiromyoides campanicus* to a nearly complete left mandible from Cernay in France. Later additional specimens were found at Cernay, and at a nearby locality, Berru[3]. The morphology of the teeth of *C. campanicus* is similar to that of *Plesiadapis* and the two genera are classified together in the family Plesiadapidae. *Chiromyoides* differs from *Plesiadapis* in having a much deeper mandible and extraordinarily enlarged upper and lower incisors (Fig. 1). These incisors are the most diagnostic elements of its dentition. The short crown length compared with root length and relatively great anteroposterior diameter of the upper incisors, together with the dorsoventral expansion and robustness of the lower incisors, distinguish them from incisors of *Plesiadapis*.

Eleven incisors and the symphyseal region of a mandible of *Chiromyoides* have been found in collections from eight North American Palaeocene localities (including the classic localities of Tiffany, Bear Creek, and the Clark Fork beds). The only complete incisor of *Chiromyoides* from North America represents a new species intermediate in morphology between the French species *C. campanicus* and early species of *Plesiadapis*.

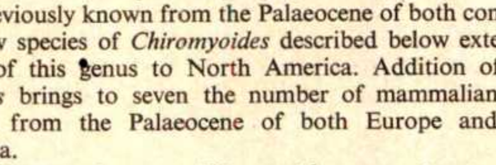

Fig. 1 Reconstruction of skull of *Chiromyoides campanicus*, based on materials described by Russell[3] and Stehlin[4]. Compare with skull of *Plesiadapis*[5,13].

Chiromyoides caesor, new species

Type: Princeton University Museum of Natural History No. 21575, a left upper central incisor collected by G. L. Jepsen from the early Late Palaeocene Croc Tooth Quarry, Section 5, T. 54 N., R. 95 W., Big Horn Co., Wyoming (see Fig. 2*a* and *c* and Table 1).

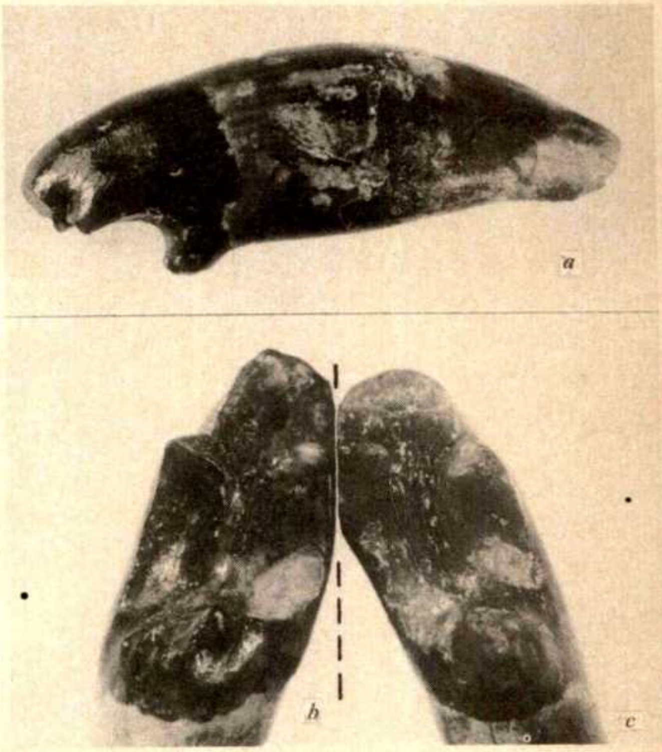

Fig. 2 Incisors of *Chiromyoides*. *a*, Type specimen of *C. caesor*, lateral view, ×4; *b*, *C. campanicus*, occlusal view, ×7; *c*, *C. caesor*, occlusal view, ×7. — — —, Midline, note medial expansion of basal cusp of *C. campanicus*. Tip of *C. caesor* incisor is worn off.

Hypodigm: Type, and University of California Museum of Paleontology No. 36652, crown of a left upper central incisor collected by T. E. Reynolds from the Mason Pocket near Tiffany, Colorado.

Diagnosis: Same size as *C. campanicus* but differs from it in having a larger, more laterally positioned basal cusp, and in lacking medial expansion of the basal cusp to form a crushing platform (Fig. 2*b* and *c*). The specific name *caesor*, L., refers to the cutting function of the incisors, which distinguishes this species from *C. campanicus*.

The lower incisors of all species of *Plesiadapis* sheared against the large basal cusps of the upper incisors as they moved between them[5]. In *Chiromyoides campanicus* the basal cusps on the upper incisors were expanded medially to form a flat crushing area, and the function of the incisors was crushing rather than cutting. *C. caesor* is intermediate in having the enlarged incisors characteristic of *Chiromyoides*, while retaining cutting incisors typical of *Plesiadapis*. Incomplete incisors of *Chiromyoides* from the Clark Fork beds of Wyoming (probably representing more than one species) are morphologically more similar to *C. caesor* than to *C. campanicus*, suggesting that the crushing specialization of the incisors of *C. campanicus* may have been confined to a separate European lineage derived from a primitive form similar to *C. caesor.*

The newly discovered mandibular symphysis of *Chiromyoides* (P.U. 19125, from beds of Tiffanian age in Wyoming and provisionally referred to *C. caesor*) is of approximately the same size and morphology as that of *C. campanicus*. The fragment includes the root of the lower incisor and the roots of PM_3. Unfortunately the crowns of these two teeth are missing. The roots of PM_3 are somewhat larger than in *C. campanicus*, indicating that the cheek teeth of *C. caesor* were larger than those of the European species.

Table 1 Measurements of the Upper Central Incisors of *Chiromyoides caesor**

	Total length (mm)	Anteroposterior diameter (mm)	Transverse diameter (mm)
P.U. 21575 (type)	19.5	6.0	3.2
U.C.M.P. 36652	—	6.1	3.2

* Diameters measured at base of crown.

The presence of species of *Plesiadapis* and now *Chiromyoides* in both Europe and North America, and the close relationship of the European genus *Berruvius* to North American *Navajovius*[3] and *Palenochtha*, indicate that the primate faunas of the two continents were probably very similar during late Palaeocene time. This is to be expected from the palaeontological and recent geophysical evidence of continental drift which suggests that Europe and North America were connected by Greenland throughout the Early Eocene[6].

Martin[7] and Cartmill[8] have published broad comparative studies on the anatomy and behaviour of living primates, and discussed the definition and classification of primates. Both authors concluded that the fossils Plesiadapoidea[9] (*Plesiadapis*, *Chiromyoides*, and their allies) differ so greatly from living Primates that they should not be classified in the same order. They did not, however, discuss the evidence on which allocation of these forms to Primates is based.

The first primates of modern aspect are found in deposits of Early Eocene age. The primitive adapid *Pelycodus*, and the primitive omomyids *Teilhardina* and *Tetonoides* seem to be stem primates close to the ancestry of the living lemurs and the tarsier, respectively. Comparison of the dentition of *Pelycodus*, *Teilhardina*, and *Tetonoides* shows them to have been closely related (which explains why the English adapid *Pelycodus eppsi* was considered for a time to be an omomyid[10]). Species of these three primitive primate genera share a number of morphological features which distinguish them from other Early Eocene mammals. The structure of the postprotocingulum ("nannopithex-fold") on the upper molars, and the relationship of trigonid cusps, together with broad talonids on the lower molars, are characteristic of the Early Eocene primate species. These features are not found in known Late Cretaceous mammals and seem to be good synapomorphous characters of primates, that is, specific characters acquired after separation of the primitive primate stock[11]. The living *Tarsius* has primitive lower molars of the *Pelycodus-Teilhardina-Tetonoides* pattern, the most uniform modification being the development of a hypocone from the primitive postprotocingulum.

The dental characteristics distinguishing primitive Early Eocene adapids and omomyids from other Eocene mammals are present in primitive plesiadapoids, and also distinguish them from other Palaeocene mammals. Thus, the most logical place to look for the common ancestor of *Pelycodus*, *Teilhardina*, and *Tetonoides* is among the Palaeocene Plesiadapoidea. The molars of Palaeocene plesiadapoids are more similar to the molars of these Early Eocene primates than to those of any other group of mammals. It is unlikely that this is a result of evolutionary convergence considering the detailed nature of the resemblance and the fact that the Palaeocene plesiadapoids immediately precede the early Eocene primates in time. If primate classification is to represent probable primate phylogeny, the Plesiadapoidea are most reasonably classified as a primitive suborder of Primates. Removal of plesiadapoids to Insectivora, as Cartmill[8] proposed, would simplify the diagnosis of Primates, but this diagnostic simplification certainly would not justify the resulting loss of phylogenetic information.

The best known Palaeocene primates (*Plesiadapis*, *Phenacolemur*, *Palaechthon* and *Plesiolestes*[12]) gave rise to now extinct side-lines of early primate evolution, but some of the smaller forms (*Palenochtha*, *Berruvius*) are still poorly known anatomically and may prove to be close to the ancestry of adapids and omomyids. Recent addition of the genus *Torrejonia*[2], and now *Chiromyoides*, to an already large North American fauna of Palaeocene primates suggests that the fauna is still not completely known. The ancestral adapid-omomyid may yet be discovered in the Palaeocene European-North American faunal province.

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Amphibious Nature of Visual Acuity in the Asian "Clawless" Otter

THE ability to acquire information at some distance and to behave accordingly increases the probability of species survival and reproduction. The propagation of light and sound differs to such a great extent in air as compared with underwater that special sensory adaptations are necessary for an animal to operate effectively in both media.

Recently there has been great interest in the amphibious nature of visual and auditory acuity in a variety of aquatic animals, including turtles[1], river otters[2], sea otters[3], mink[4], porpoises[5], pinnipeds[6] and man[7,8]. The latter, for example, shows an expected 20 dB hearing loss under water[7]; also when not wearing goggles the loss of refractive power of the cornea under water[9] cannot be sufficiently compensated by the accommodative power of the lens so that, at a distance of 0.7 m, human visual acuity in water suffers an eight-fold decrease compared with that in air, and at a distance of 5 m humans are virtually unable to resolve sufficient detail to differentiate form from background[8]. Thus man, like other terrestrial mammals that have not developed special adaptations for seeing under water, is hypermetropic in water while being emmetropic in air. On the other hand, truly amphibious mammals like the pinnipeds, which feed exclusively under water and carry out many reproductive functions on land, have essentially an emmetropic eye under water while possessing special dioptric mechanisms for seeing detail in air.

Pinnipeds have developed a permanently changed curvature of the lens for seeing under water. On the other hand, otters are thought to have a similar device to turtles, in having well developed ciliary and sphincter muscles which squeeze the anterior part of the air adapted lens, giving it a focal length similar to that of a spherical lens[8].

The visual acuity of the Asian "clawless" otter has been measured both in air and under water under a light intensity level of 100–200 mL (ref. 2), and it was found that the closest grating spacings that could be resolved in both media subtended visual angles ranging from 14–16 arc min. As this special adaptation of otter underwater vision is thought to be achieved primarily by the action of the powerful iris sphincter closing down on and distorting the lens, a question arises as to the effects of ambient light on the iris sphincter. If the pupil fully dilates under low light levels, then the lens would not become sufficiently spherical, thus resulting in the otter's eye becoming hypermetropic in water. This would in turn lead to the hypothesis that as luminance decreased under water, visual acuity in otters would deteriorate at a more rapid rate under water than it would in air. To test this, we measured the aerial and underwater visual acuity of two mature male Asian "clawless" otters (*Amblonyx cineria cineria*) in three ambient light conditions.

The testing tank apparatus, general testing procedures and acuity targets were the same as those used previously[2]. Acuity targets were produced from 12.7^2 cm photos of Ronchi rulings with black and white stripes of equal width. The standard grating consisted of 300 lines per inch, the variable gratings of lines varying in width from 12.7 mm to 4.8 mm. Targets were presented simultaneously by lowering a target board from behind an opaque screen. The only modifications were to control ambient light intensities, simply by covering the top of the apparatus with a double layer of 8 mill black vinyl sheeting. The amount of light entering the tank and reflected from the targets was controlled by opening the top cover a given amount. At the start of each test session the experimenter dark adapted and an assistant would then slide back the black vinyl cover until the desired light level was obtained. The light intensities were 0.3, 0.03 and 0.009 mL. Daily light readings were taken with an SEI meter which was checked against a Macbeth illuminometer.

The otters were maintained at fixed distances of 1.7 m and 1.3 m at the highest light level, 1.3 m at the next highest light level and at 0.76 m at the lowest light intensity. A modified psychophysical method of limits was used to obtain visual acuity thresholds.

In most conditions each animal's threshold was defined as the interpolated values at which the animal responded correctly 75% of the time. If an otter never achieved a value of 75% correct responses or better, however, then the threshold was defined in terms of visual acuity targets resulting in discrimination performance which was significantly better than chance ($P<0.01$).

At each test session ambient light levels remained relatively constant, and stripes were made finer if the animal succeeded in making seven or more correct responses in ten successive trials. The otters were dark adapted 30 min before each test session.

The main results of the experiment (Table 1) clearly support the idea that visual acuity in otters, although showing an air-water equivalence in relatively bright light, degrades at a considerably more rapid rate in water than in air. The lack of visual accommodation in otters under water in the dark may be due to pupillary dilation resulting in insufficient squeezing of the anterior portion of the lens by the iris sphincter muscles. On the other hand, one might argue that the present findings are not due to the lack of lens accommodation, but result from insufficient pupillary dilation in the dark, thus reducing the amount of light entering the submerged eye. This explanation assumes that squeezing of the lens by the pupil aperture occurs either voluntarily or is triggered reflexively soon after the otter goes under water.

Table 1 Aerial and Underwater Visual Acuity Thresholds* as a Function of Ambient Light Levels

Luminance (mL)	River otter, Tom		River otter, Jerry	
	Air	Water	Air	Water
100–200†	14	15	15	16
0.3	18	18	17	17
0.03	23	33	23	33
0.009	39	57	38	58

* In minutes of visual angle.

† Data from Balliet and Schusterman[2].

It is interesting to compare the present experiments with otters whose eye is emmetropic in air with special adaptation for seeing under water, with similar experiments using seals and sea lions whose eyes are emmetropic under water with special adaptations for seeing in air.

In the California sea lion (*Zalophus californianus*) aerial acuity deteriorated at a much more rapid rate than underwater acuity in the luminance range of 3 to 0.000003 mL (ref. 6). These results are consistent with the idea that as pupil size in seals and sea lions varies with ambient light intensity regardless of whether the eye is submerged[10], the narrow vertical slit pupil in air provides good visual acuity in relatively brighter light, but in dim light the pupil is dilated and aerial visual acuity is reduced by the astigmatism of the cornea. Although the pupil is dilated under water, the corneal astigmatism of sea lions plays virtually no role because of the similar refractive indices of the cornea and water.

Thus a comparison of the effectiveness of the visual systems of modern aquatic mammals suggests that only when tested under a wide range of lighting conditions is there a correlation between the degree of adaptedness of different amphibious species to aquatic and terrestrial habitats.

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Changes in Fishing Ability of Terns associated with Windspeed and Sea Surface Conditions

THE terns are a group of largely marine fish-feeders, many of which obtain their prey by skilful air-to-water plunge diving. Previous observers have assumed that light winds and rippling of the water surface either have no effect[1] on the fishing success of terns or else are detrimental[2], but there has been no direct evidence to support either view. To investigate this problem, a study of Sandwich terns (*Sterna sandvicensis*) and common terns (*Sterna hirundo*) was carried out in Northumberland, England.

Both species were easily observed as they foraged close inshore, diving from heights of 3–10 m. The tern, if successful, emerged from the water with its prey held conspicuously in its bill. Daily fishing success (percentage of plunge dives yielding prey) was derived from several hours' observations involving many different birds. Plunge diving rates were obtained by timing individual bouts of feeding activity (for 2–10 min). The sea surface conditions encountered in the foraging area were classified by presence or absence of ruffling as either "calm" (=surface smooth or slightly rippled ± light swell) or "moderate" (=windchop ± light swell). Windspeeds (in knots; 1 knot=1.85 km h^{-1}) were obtained from a meteorological station situated 4.8 km inland from the main study area.

So as to eliminate the known effects of tidal movements[3,4] fishing ability is compared over an equivalent part of the tidal cycle on different days. In 1968 and 1969 the fishing success of both species was better in moderate than in calm seas (Table 1). Although overall success was appreciably higher in 1969, the proportional improvement from calm to moderate conditions was similar for both species in the two years. Furthermore, the fishing success of the two terns was directly correlated on a day-to-day basis ($P<0.02$). A comparison of capture rates (Table 2) takes account of the birds' tendency to dive at a faster rate in moderate than in calm seas.

Table 1 Mean Daily Fishing Success (± 1 s.e.) in Calm and Moderate Sea Conditions

	Calm			Moderate		
	Success (%)	Days	Dives	Success (%)	Days	Dives
Sandwich tern						
1968	11.0±1.5	5	504	16.8±1.5	6	535*
1969	35.7±1.5	4	411	57.5±5.5	4	362†
Common tern						
1968	17.0±4.4	4	265	27.9±5.4	3	212 n.s.
1969	21.9±2.6	4	156	38.9±6.0	4	191*

* = *P* success <0.05. † = *P* success <0.01. n.s. = *P* success not significant.

For Sandwich terns both fishing success and capture rates (Fig. 1*a*) were directly correlated with windspeed ($P=0.02$, $P<0.02$ respectively) whereas plunge diving rate was not. These correlations raise the problem of distinguishing the effects of wind *per se* from those of related surface conditions. The extent of surface disturbance is not, however, directly related to prevailing windspeeds. A choppy sea, for example, persists after the wind responsible has abated. Again, an onshore breeze may produce a moderate sea inshore, whereas a calm sea may occur with an offshore breeze of the same strength. Such effects allowed a comparison of capture rates in a variety of windspeeds with differing surface conditions for each. For any particular windspeed, moderate conditions were generally associated with a higher capture rate than calm conditions (Fig. 1*b*). Although neither the "calm" nor the "moderate" regression is significant, they are approximately parallel and their 95% confidence limits differ in elevation between 8–11 knots. This suggests that surface conditions may contribute independently of windspeed to influence fish capture rates of Sandwich terns. None of these differences in fishing ability was correlated with variation in cloud cover.

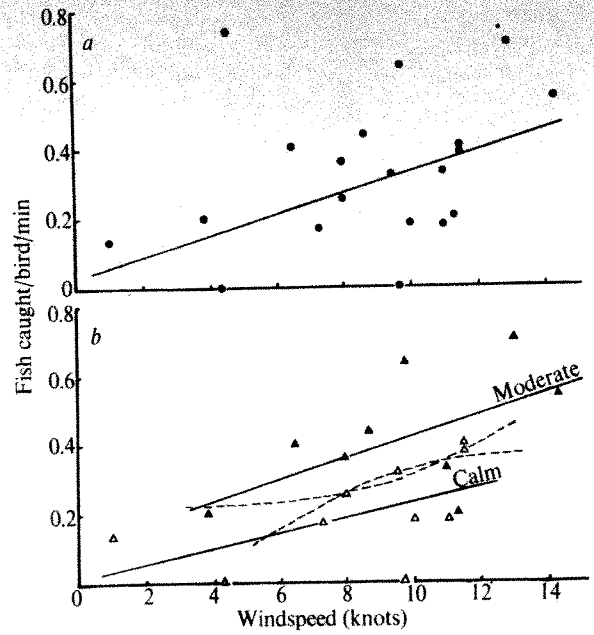

Fig. 1 Prey capture rates of Sandwich terns in different windspeeds. In (*a*) no distinction is made for sea conditions and a single regression line ($y=0.03x+0.03$) is shown ($P<0.02$). In (*b*) separate regressions are calculated for calm (△) ($y=0.02x+0.01$) and moderate (▲) ($y=0.03x+0.11$) sea conditions. The 95% confidence limits are shown by the broken lines.

Table 2 Mean Daily Rates of Prey Capture (±1 s.e.) in Calm and Moderate Sea Conditions

	Calm		Moderate	
	Prey min^{-1}	Prey h^{-1}	Prey min^{-1}	Prey h^{-1}
Sandwich tern				
1968	0.10±0.04	6	0.29±0.04	18†
1969	0.32±0.05	19	0.73±0.11	44*
Common tern				
1969	0.23±0.02	14	0.50±0.08	30*

* = *P* prey $min^{-1}<0.05$. † = *P* prey $min^{-1}<0.01$.
Prey h^{-1} are extrapolations assuming sustained foraging activity.
No common terns were timed in 1968.

Various authors[1–6] have noted that in stormy conditions terns experience difficulty in obtaining food, probably because it is hard to maintain an accurate diving trajectory and because fish may remain further below the surface. It has not previously been realized, however, that within a certain range, increasing windspeed produces conditions which facilitate fish capture. I suggest therefore that these conditions reach levels that optimize fishing ability after which their effects are increasingly detrimental to the birds. It only remains to explain the initial improvement in fishing ability. First, most plunge dives are preceded by hovering and it appeared that the less wind there was, the more vigorously did terns have to hover in order to remain stationary. Fish can probably detect and respond to movement of terns hovering a few metres above the surface[7]. Prey may therefore have a better chance of spotting terns on still days which demand concerted hovering effort. Second, the fish caught are much closer to the water surface than the tern and it is probable that with increasing disturbance the surface acts rather like a sheet of frosted glass to impair the fish's view of the tern much more than the tern's view of the fish.

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Mitosis in the Cryptophyceae

Recently a number of papers have been published describing the fine structure of nuclear division in the algae. This interest has no doubt been stimulated by the great variety of nuclear structures found and their relevance to current discussions on algal phylogeny[1–3]. In the past year we have had the first detailed accounts of mitosis in the Chrysophyceae[4], Xanthophyceae[5], Chloromonadophyceae[6], Rhodophyceae[7], and Phaeophyceae[8]. This leaves only three classes, Prasinophyceae, Eustigmatophyceae and Cryptophyceae in which details of mitosis are unrecorded. We would like to help complete the picture of algal division by making known some recent findings about mitosis in a member of the Cryptophyceae, *Chroomonas salina* (Wislouch) Butcher.

Mitosis in *Chroomonas* is characterized by the following features. (1) Before the start of mitosis the flagellar bases divide. Microtubules extend from the flagellar bases to the area of cytoplasm around the nucleus. These seem to be randomly arranged and are often very close to, or in contact with, the nuclear envelope. (2) As the nuclear envelope breaks down the microtubules extend into the nucleus. The chromatin aggregates into a pear shaped mass through which pass tunnels free of chromatin. This is interpreted as a part of prophase. (3) The nuclear envelope breaks down but areas of nuclear envelope material may remain. The extent and positioning of this material are variable. The area in which mitosis occurs is roughly delimited by sheets of endoplasmic reticulum. (4) At metaphase the chromatin is aggregated into a dense plate on the equator (Fig. 1*a*). Many spindle microtubules pass through channels in this plate and others seem to connect with the chromatin mass. No kinetochores were seen. (5) No centrioles or spindle organizing bodies appear to be present though microtubules can occasionally be seen to contact the endoplasmic reticulum surrounding the mitotic area. No connexion was seen between the flagellar bases and the spindle microtubules at metaphase or anaphase. (6) At anaphase two dense clumps of chromatin separate. Individual chromosomes cannot be distinguished in these clumps (Fig. 1*b*). (7) In telophase the chromosome clumps appear to be pushed back into the endoplasmic reticulum sheath surrounding the chloroplasts and this appears to form the first part of the nuclear envelope. New nuclear envelope material seems to be formed on the opposite side of the nucleus.

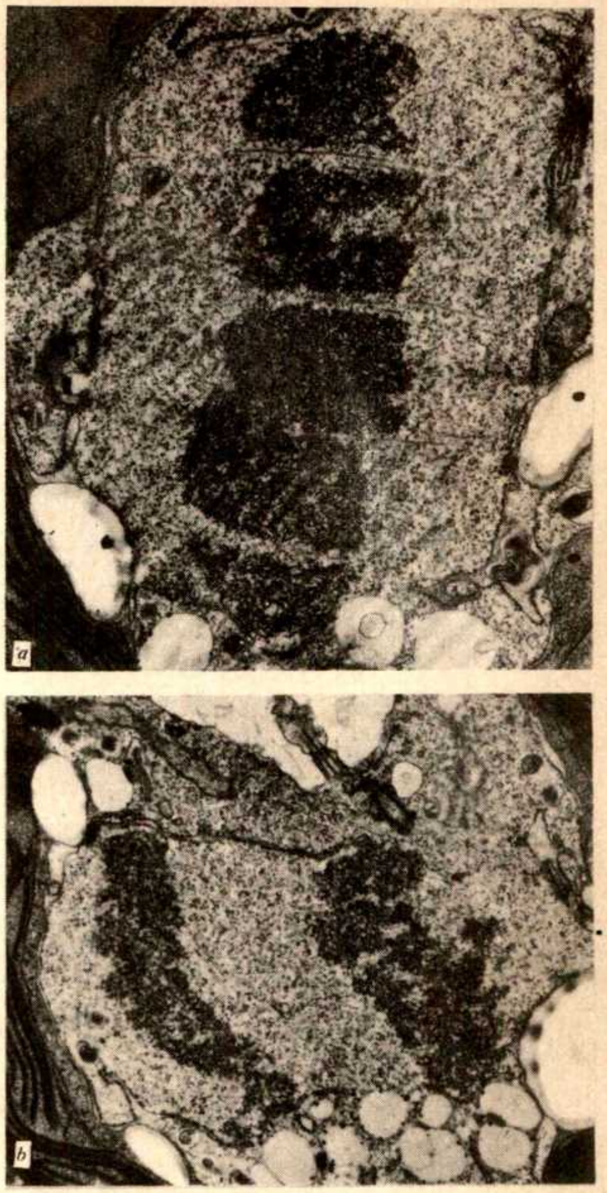

Fig. 1 *a*, A section through a metaphase of *Chroomonas* showing the chromatin aggregated into a dense plate on the equator. A number of the spindle microtubules can be seen to pass through channels in the plate. × 17,000. *b*, A similarly orientated section through an anaphase of *Chroomonas* showing the chromatin separating in two dense masses. Individual chromosomes cannot be distinguished. × 9,350.

Early light microscopic work on another cryptophyte, *Chilomonas paramecium*, suggested that true chromosomes did not exist[9–11]. Later microscopical work reported, however, that this organism possessed many very small chromosomes[12]. Our work suggests that on an ultrastructural level, multiple chromosomes cannot be distinguished, though the tunnels through the metaphase plate might give the impression that there were many distinct chromosomes if a section through only one plane was examined, or possibly if the nucleus was squashed before examination. It would be very interesting to see if the chromatin behaves genetically as one chromosome pair.

This form of mitosis is clearly distinct from that of the Dinophyceae[13], to which the Cryptophyceae were thought to be closely related. It is also quite different from that of the

Rhodophyceae[7] which has certain similarities of pigmentation. It appears to resemble most closely the mitosis of *Prymnesium* (Haptophyceae)[14] and to have some similarities with that of *Ochromonas* (Chrysophyceae)[4]. In the endosymbiotic scheme for the origin of plastids and phylogeny of algae proposed by Lee[15], the Cryptophyceae were thought to be ancestral and closely related to the Cyanophyceae. Our findings show no evidence, however, for a primitive condition in nuclear or mitotic structure. It would seem possible that the mitotic process may give quite a different phylogenetic picture from that obtained with chloroplast structure and pigmentation.

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Linguistic Structure and Speech Shadowing at Very Short Latencies

SPEECH shadowing is an experimental task in which the subject is required to repeat (shadow) speech as he hears it. When the shadower is presented with a sentence, he will start to repeat it before he has heard all of it. The response latency to each word of a sentence can therefore be measured.

The response latencies reported[1,2] for the accurate shadowing of continuous prose typically range between 500 and 1,500 ms. These latencies may be compared with those obtained in reaction-time (RT) experiments in which the subject repeats isolated words or nonsense syllables. In such studies[3-7], the RT's are of the order of 150 to 250 ms. This difference in RT's may seem to reflect differences in complexity between sentences and lists of isolated items for, according to modern psycholinguistic theory, higher order linguistic structure plays an essential role in the process of speech perception. Such higher order structure (syntactic and semantic) is defined over units of analysis at least as large as a phrase. Thus, to use this information, the shadower would not be able to respond until he had heard at least a phrase, and should therefore have longer repetition latencies to prose material than to unstructured lists.

This report establishes that it is possible, however, to shadow continuous prose accurately at latencies as short as those found for isolated items, and examines the question of such shadowers' use of higher order linguistic structure.

Sixty-five subjects were screened in a search for individuals who could shadow closely while still repeating the material clearly. Seven of these proved capable of shadowing at mean delays of 350 ms or less while still maintaining the intelligibility of their speech. All the other subjects were only able to shadow clearly at rather longer latencies (500–800 ms).

The seven close shadowers, together with seven of the more distant shadowers, then shadowed a pair of 300-word passages of normal prose read at a normal conversational speaking rate (160 w.p.m.)[8]. The passages were presented binaurally through headphones. The subjects' production was recorded onto one track of a tape-recorder, while the material they were hearing was simultaneously recorded on a second track. For each passage, the repetition latency was measured from a polygraph tracing of the two records, always at the beginning of an easily identifiable word. The seventy-five measurement points were distributed equally over the passage at different serial positions within sentences, and were the same for all subjects.

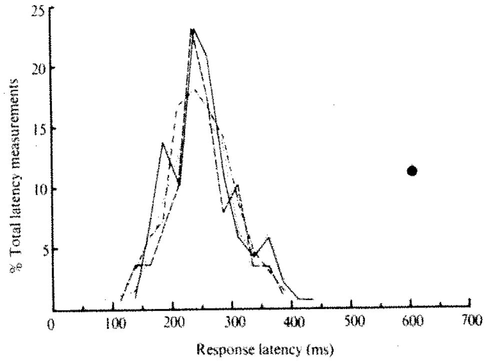

Fig. 1 The distribution of latencies for four very close shadowers.

Of the seven close shadowers, the response latencies of the four closest are plotted in Fig. 1. The mean latencies of these four shadowers ranged between 254 and 287 ms, with standard deviations of between 54 and 85 ms. Their error rates ranged from 1.7 to 6.6%.

In comparison, the responses of two of the less close shadowers and of two of the distant shadowers are plotted in Fig. 2. These curves are typical of those found for subjects not shadowing consistently at very short latencies. The mean latencies for these subjects were 305, 362, 559 and 600 ms respectively. The standard deviations ranged between 85 and 129 ms, with error rates of 0.5 to 5.8%.

The mean syllable duration for material read at a rate of 158 w.p.m. is 200 ms (ref. 9). Thus, to shadow at a distance of 250 ms is to remain little more than a syllable behind the original material. We know that it is possible to repeat isolated syllables with similar or even shorter delays. This suggests that the closest shadowers are processing the incoming material at the level of individual syllables. Such a mode of speech analysis needs to be reconciled with the recent psycholinguistic emphasis on the importance of syntactic and semantic structure in speech perception.

If the close shadower is not using syntactic and/or semantic structure, then he should not have available to him information that could only derive from these levels of analysis. One way of testing this is to question the subject about the content of a passage he has shadowed. Thirteen of the fourteen subjects were given a further passage to shadow, 600 words long and again presented at 160 w.p.m. They were not told in advance that they would be given a memory test. Immediately following the passage, they were asked a series of questions about it. The results showed very little relation between latency and memory for content. There was a small, nonsignificant, negative correlation ($r=0.18$) between increasing latency and memory score. No difference was found between the scores of the shadowers and a control group of listeners.

The results of the memory test show that syntactic/semantic information is available to the shadower irrespective of his shadowing latency, but this does not exclude the possibility that the shadower performs the higher level analysis of the material after he shadows it. The close shadowers could produce their output on the basis of a low level analysis and perform the rest of the analysis later. Such a procedure should be reflected in the subjects' errors.

If the shadower's performance is based, for example, on a syllabic analysis of the material, then his errors should be constrained by the syllabic character of the material, but not by its semantic or syntactic character. Furthermore, if the relative distance of an individual's shadowing performance is a function of the "depth" to which he analyses the material, then there should be latency-dependent differences in the types of errors which the subjects make.

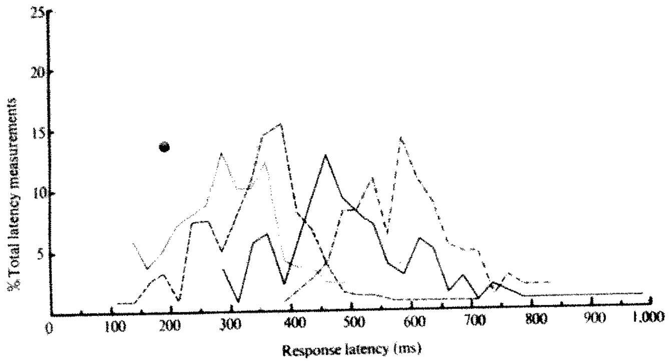

Fig. 2 The distribution of latencies for four subjects shadowing at distances greater than 300 msec.

The errors made on the two passages of normal prose were therefore analysed. Of the total of 402 errors made by the fourteen subjects, 221 were delivery errors (slurring, hesitations, etc.), 49 were omission errors, and 132 were constructive errors in which subjects either added or changed entire words, or changed part of a word so as to make it into a different word. Twenty-one of the latter resulted in syntactically/semantically unanalysable nonsense words.

The remaining 111 constructive errors were analysed according to their grammatical suitability with respect to the preceding context. Of these, only three were structurally inappropriate. All the other errors were both semantically and syntactically congruent with the preceding context. A regression analysis showed there to be no systematic relationship between shadowing latency and grammaticality of errors. Although the closer subjects tended to make more errors overall ($t=2.403$(d.f.$=13$), $P<0.025$), this difference derived more from the delivery errors ($t=2.308$(d.f.$=13$), $P<0.025$) than from the constructure errors ($t=1.411$(d.f.$=13$), $P<0.10$). Indeed, if each subject's total grammatical errors are expressed as a proportion of his total errors, then one finds no latency-dependent differences at all ($t=0.248$(d.f.$=13$), $P<0.50$). These results are not consistent with the idea that higher order structure is not available at very short latencies.

The constructive errors of close and distant shadowers are also qualitatively very similar, and indeed the same errors were sometimes made by subjects in both groups. For example, in the sentence "It was beginning to be light enough so I could see . . .", two subjects inserted the deleted "that" following "so": one shadowing at 254 ms, the other at 559 ms. In the sentence beginning "He had heard at the brigade . . .", five subjects replaced "heard at" with "heard that": their latencies were 264, 287, 362, 444, and 553 ms. Nor do these errors occur only when the subject's shadowing delay is longer than usual. These errors, especially in the case of the closest shadowers, usually occur when the subjects' latencies are shorter than average, as if they are placing more reliance on the predictive properties of the higher order context.

These examples, and the errors in general, also show that the subjects' output can be constrained by the preceding context up to and including the word immediately before the error. The error "that" in the first example is clearly contingent on knowing that the preceding word is "so". Similarly, in the second example, the subjects would need to have extracted the structural implications of "heard" to make the grammatically appropriate error of saying "that" instead of "at".

There seems to be no difference between close and distant shadowers in their use of the semantic and syntactic information available. The data suggest that all the subjects analyse the material up to a semantic level as they repeat it, and that this analysis helps to determine the ongoing series of perceptual decisions underlying their shadowing performance. The significance, therefore, of very close shadowing is not that it indicates some anomalous minimal mode of speech processing, but that it seems congruent with what we know of normal speech perceptual processes. The present results, in these terms, pose problems for any theory of speech perception which requires that the assignment of higher order structural descriptions await the end of a major constituent.

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Axenic Culture of a Plant Pathogenic Spiroplasma

EVIDENCE has accumulated that a number of insect-transmitted plant diseases of the "yellows" group result from the infection of plants by organisms resembling mycoplasmas[1,2]. Circumstantial evidence suggests that two such diseases, corn stunt and citrus stubborn, may be caused by a novel type of helical prokaryotic microorganism lacking a cell wall, for which the trivial name "spiroplasma" has been proposed[3]. The agent of corn stunt has so far defied attempts at culture in a cell-free medium and although an organism associated with citrus stubborn disease has been successfully cultured from diseased plants[4,5] it has not, to our knowledge, been shown to be a plant pathogen.

Citrus little-leaf, a similar disease to citrus stubborn, was first observed in Palestine in 1928[6]. No insect vector has yet been identified. Zelcer *et al.*[7] have observed mycoplasma-like organisms in electron micrographs of ultrathin sections of infected plants.

"Lop-sided" fruits from sweet orange trees (*Citrus sinensis* cv. Valencia) with little-leaf disease were washed and surface-sterilized with 70% (v/v) alcohol. The aborted seeds were then removed aseptically and rinsed in sterile water. Seed coats were selected for study because it is known that the citrus stubborn agent may be cultured from this tissue[8]. They were ground with sand in the growth medium of Saglio *et al.*[5], containing the selective agents 'Floxapen' (Beecham) 50 µg ml^{-1} and, in later experiments, thallous acetate (0.05%, w/v). The extracts were then centrifuged at 500*g* for 2 min to remove debris and filtered through sterile 'Millipore' membrane filters (0.45 µm pore diameter). The filtrate was diluted with further growth medium and incubated at 32° C. Portions were also streaked and incubated on plates of medium solidified with 1% 'Ionagar' No. 2 (Oxoid).

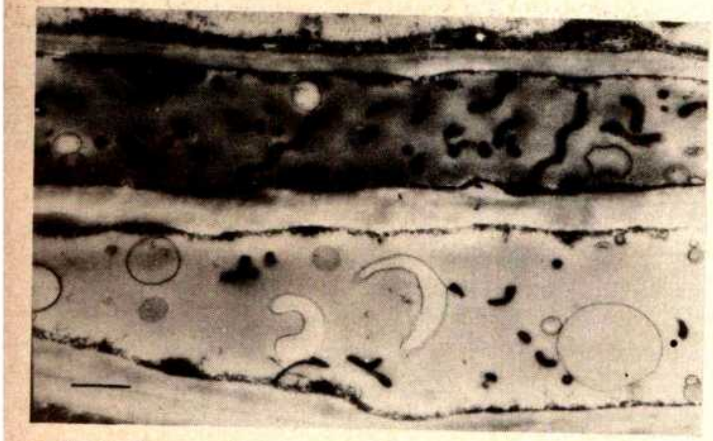

Fig. 1 Electron micrograph of a section (about 150 nm thick) of phloem in a petiole from an infected clover plant showing spiroplasmas in sieve tubes. The scale bar represents 1 µm.

After 7–10 d, slight turbidity was noted in the liquid cultures and acid production was shown by a change in colour of the phenol red internal indicator from red to yellow. Examination by phase-contrast microscopy revealed large numbers of delicate helical filaments about 0.2 µm in width and up to 15 µm long, exhibiting the type of whirling and flexing movement described by Davis and Worley[3] for the corn stunt spiroplasma. Small colonies (about 0.1 mm diameter) having the "fried egg" appearance typical of mycoplasma colonies were observed on plates. Electron micrographs of thin sections of colonies and of organisms centrifuged from broth cultures showed that the filaments were bounded only by a unit membrane, no traces of external cell wall material being seen. Their appearance was identical with that of the organisms shown in Fig. 1. We found no reversion to walled forms when the spiroplasmas were grown in the absence of penicillins.

We received seven batches of fruit showing symptoms from separate trees and were able to culture spiroplasmas from all of them. In contrast, no isolations were achieved from a number of samples of healthy fruit from several sources. Heating the seed coat extract to 40° C for 20 min, before dilution with further growth medium, completely prevented growth of the spiroplasmas.

After serial subculture equivalent to a dilution of the original diseased plant extract by a factor of at least 10^{25}, broth suspensions of spiroplasmas were injected into leafhoppers (*Euscelis plebejus* (Fallén)) known to act as vectors of some European yellows type diseases. The insects were caged in groups of forty on white clover plants (*Trifolium repens* L. var. S100) at 25–30° C. After about 5 weeks four out of seven test plants developed severe symptoms of chlorosis followed by stunting and dwarfing of young leaves. No such symptoms were observed on a large number of control plants maintained insect-free, or on those exposed to insects which were either uninoculated or injected with sterile broth. Electron microscopy demonstrated the presence of many spiroplasmas in phloem tissue of the infected plants (Fig. 1), but not in healthy plants. We were able to culture spiroplasmas from the insects for at least 10 weeks after injection, and we reisolated the organisms from the infected clover plants. The pathogenicity tests were repeated, with similar results, using further spiroplasma subcultures.

Our experiments have demonstrated the association of spiroplasmas with the plant disease, citrus little-leaf. We have cultured the microorganisms and by using an insect as a vector we have been able to show for the first time that spiroplasmas are plant pathogens. We are at present attempting to transmit the organisms to citrus plants in order to fulfil Koch's postulates and prove, as seems highly probable, that spiroplasmas are the aetiological agents of citrus little-leaf.

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Reference Abbreviations

From September 1 it is *Nature's* intention that all abbreviations of references should conform to the style of the *World List of Scientific Periodicals*, fourth ed. (Butterworth, 1963–65). The changeover will be gradual and authors submitting manuscripts from now on are asked to ensure that the references are written appropriately.

BOOK REVIEWS

Hoyle on Copernicus

Nicolaus Copernicus An Essay on his Life and Work By Fred Hoyle Pp vii+94+6 plates (Heinemann Educational London, May 1973) £1 50

NEARLY everyone is ready to honour Copernicus, yet very few can explain exactly what he achieved "His heliocentric picture of the solar system was the beginning of modern science" is the kind of cliché that hides several half-truths The heliocentric picture was propounded by Aristarchus of Samos nearly 1,800 years earlier does Copernicus deserve much credit for merely reviving it? Paradoxically he does, because he had to face a greater obstacle than Aristarchus, namely the entrenched dogma in favour of the geocentric theory, built up over many centuries But even in ancient times the idea of planets elegantly circling the Sun was abandoned because it did not fit the facts well enough, and Ptolemy's inelegant but effective system of epicycles came to prevail The achievement of Copernicus was to devise a heliocentric system that described the planetary motions as well as Ptolemy's (or almost as well), yet also held the potential for fruitful mathematical development in the hands of Kepler and Newton

Fred Hoyle has now written an admirable little book clearly explaining the achievements of Copernicus for anyone who is prepared to follow some straightforward equations The main difficulty in writing about Copernicus is to make a detailed comparison with Ptolemy, and Hoyle does so by expressing the radius vector of a planet as a complex number, expanding in powers of the orbital eccentricity e and (generally) neglecting terms in e^2 Interpreted geometrically, the results show clearly the similarities and differences between the Copernican and Ptolemaic systems, but without the elaborate constructions which so often baffle modern readers (Incidentally, Ptolemy comes out of the comparison very well) Although this is the crux of the book, the earlier chapters usefully prepare the way by describing the Aristarchan heliocentric system In addition there is a 23-page biographical chapter—not just a re-hash of the standard biographies of Copernicus, but a fresh look In Hoyle's view, the idea that the Earth rotated was accepted by Copernicus before he was 30, but he only began serious quantitative work on the solar system when he was 40, and the theory was fully developed in his fifties, between 1523 and 1533

The book is attractively written and animated by a light personal touch, to remind us that

> True ease in writing comes from art,
> not chance,

—in this instance the novelist's art I strongly recommend the book as a guide to Copernicus for any reader with a modicum of mathematics

D G KING-HELE

What is Science?

What Is Science For? By Bernard Dixon Pp 255 (William Collins London, July 1973) £2 50

THE avowed purpose of this book is to provide "an assessment of what science is and how scientists work" The author is a leading member of a profession that is bound to become more and more important as science becomes more and more complicated and scientific considerations weigh ever more heavily in political decisions Although the passage is amusing and not unjust, the author is unwise to start off by describing characteristics he most dislikes in a reviewer, because this is asking for retaliatory comments Perhaps the reviewer specially dislikes an author who chooses as the title of his book a question which (unlike, say, "*was Metternich a negro?*") hardly admits a straightforward answer But, of course, if the answer had been straightforward there would have been little incentive to write a book

Dixon starts with an account of the degree of esteem or disfavour in which science has been held from the 17th century to the present day, and he calls attention emphatically but temperately to the activities which have made people see an essential malignancy and have given them a "a new fear of positive evil" in the pursuit of science, he draws a parallel beween the bewilderment of modern scientists at their current revaluation by society and the doubts and bewilderment of the clergy at that reappraisal of their status for which science itself was responsible, but it was ill-judged to use the term "corporate menopause" to describe the condition of the scientific profession today, because there is no evidence that scientific productivity is declining or on the point of giving out Next "What is a Scientist?" and "is there indeed such a definable figure?" A number of witty case-histories make it clear that scientific activities and the people who carry them out are remarkably diverse What Dixon says is always pointed and interesting, as a good journalist's writing ought to be, and in spite of occasional pinpricks most scientists will probably regard his account of the matter as a just one The same goes for his account of what actually goes on in the mind when scientists practise what laymen obstinately believe to be "the" scientific method So far from being the practitioner of one cut and dried method, he sees the scientist as the practitioner of a certain way of life—a man who by systematic research and occasional imaginative forays but above all by the habit of self-correction builds up interpretations of the world which are ever more trustworthy and reliable and come ever closer to what is called "the truth"

Dixon fully understands and gives due weight to the importance in scientific life of the scientific community, the *internationale* of fellow professionals who scrutinize each others' work, correct it and carry it on "Scientists of the world unite," Henry Tizard, England's leading scientific administrator, was fond of saying at the end of the Second World War, when it looked as if national rivalry and political ambition between them would do us all in Actually, we have an *internationale* already but it is a purely professional one and carries no political weight Thus we shall have to take Lord Zuckerman's advice and become politicians ourselves if we are to influence policy in any effective way Unfortunately, Dixon's badly overwritten section on research funding with special reference to the Rothschild report illustrates the worst of journalism as clearly as the rest of his book exemplifies the best of it, but he has some useful and pointed things to say on "grantsmanship" and how certain non-scientific talents may conduce to getting research support

Though Dixon disclaimed any intention to write a "scholarly" work he is in fact very well read, intelligent and fair minded and that is the more important part of scholarship anyway Though scientists come in for some pretty plain speaking, nothing is said that will shake their basic faith in scientific meliorism—the belief that the world has been and may yet be made a better place to live in as a result of scientific research

P B MEDAWAR

Dedicated to Dirac

Aspects of Quantum Theory Edited by Abdus Salam and E. P Wigner Pp xvi+268 (Cambridge University London, November 1972) £7 10, $23 50

THIS is not just one of the many *Festschriften* which are now following each other in quick succession as the pioneers of twentieth century physics inexorably reach their sixtieth or seventieth birthday The editors of this volume, dedicated to Dirac, have spared no effort to make it, not only a fitting tribute to one of the greatest of these pioneers, but a significant contribution, of lasting value, to the history of the heroic period of quantum theory After a complete bibliography of Dirac's publications, the book opens with three biographical articles The last of these, by J Mehra, manages with remarkable psychological insight and literary talent to give a true-to-life picture of Dirac's unique genius and lovable personality, the preceding reminiscences of Van Vleck are, in a lighter vein, quite entertaining and as revealing of the author's as of his hero's character as travellers out of the beaten track in the Rockies and elsewhere Then comes a sequence of twelve more specialized articles, authoritatively treating of the great problems of quantum theory to which Dirac's name is attached, these contributions are not strictly historical, they offer original views of their eminent authors on the problems in question and their later developments There would be little point in commenting on them all, each reader will find some of them more to his taste than others Personally, I found extremely valuable Wigner's considerations on the time-energy uncertainty relation, and thoroughly enjoyed Laurent Schwartz's candid confession of initial scandal when he learned of the "δ-function" and of frightened surprise when he much later saw what the physicists had managed to achieve by manipulations of "distributions"—without being "entitled" to do so by the mathematicians

L ROSENFELD

Physics of Atoms

Atomic and Nuclear Physics By John Yarwood Pp 608 (University Tutorial Press London, 1973) £3.90

IN recent years it has become the fashion in many university physics courses to introduce atomic and nuclear physics with a large dose of quantum mechanics and in this way to instil some of the difficult theoretical concepts at an early state in an undergraduate's career Such courses have a great attraction for those with strong mathematical leanings but of necessity the emphasis on theory has relegated the historical and experimental aspects of the subject very much to second place It is, therefore, interesting to find this new book on atomic and nuclear physics which adopts the unfashionable approach with the emphasis on experiments and on the elementary principles underlying them Tackling the subject in this way makes rather less demand on the mathematical ability of the reader and yet enables him to familiarize himself with many of the phenomena on the atomic and subatomic scale and to learn something of the techniques used in their study

The first half of the book is concerned with atomic physics which is approached through mass spectroscopy, atomic structure and the elements of wave-mechanics it also includes chapters on X radiation and atomic magnetism A very considerable amount of material is covered and the accounts of experiments contain valuable detail which is so often omitted in textbooks It is perhaps surprising that little mention is made of the photoelectric effect which historically played such an important role in the development of ideas on the particle nature of light, and the sole reference is to the part it plays in the attenuation of an X ray beam. The second and larger half of the book is devoted to nuclear physics which is introduced through natural radioactivity and the properties of radiations It then proceeds through chapters on particle accelerators, detectors and nuclear fission to nuclear structure, reactions and elementary particles The strongly experimental flavour is reflected in the considerable space devoted to neutron physics and its application to reactors Again the coverage is broad and most of the important phenomena of nuclear physics are included and well described.

Although there are several significant errors of physics in the book, this is perhaps hardly surprising in a work which is so wide-ranging The topics are treated concisely and readably and a wealth of material is contained in this relatively inexpensive book It is certain that if it were on the shelves of a library it would be used by undergraduates because of the clear and simple way in which the information is laid out As a course textbook, however, it is likely to be of most value where quantum mechanics plays little part in the course

M A GRACE

African Gastropods

Sea Shells of Southern Africa—Gastropods By Brian Kensley. Pp 225 (Maskew Miller Cape Town, in collaboration with the South African Museum, 1973)

SOUTH AFRICAN shores stretch for a distance of well over 2,000 miles and include four climatic zones with the Benguela Current extending cold conditions well up the east coast and the Mocambique and Agulhas Currents on the west bringing semi-tropical conditions as far south as Durban and warming the southern shores The diversity of the shore populations was fully described in pre-war surveys made by the late Professor T A Stephenson

Although a few shells from South Africa were named by Linnaeus and Lamarck, systematic collection did not begin until the middle of the last century largely by British and United States survey vessels These were later extended by the Challenger and the Valdivia which trawled and dredged to some depth Collection by local trawlers had begun by the end of the century

British conchologists, notably G B Sowerby (the third), E A Smith and J R le B Tomlin, played a notable part in establishing on a sound basis the taxonomy of South African marine Mollusca This was followed by the impressive contributions between 1951 and 1964 of K H Barnard of the South African Museum

There have been unfortunate episodes in South African conchology, notably the entirely uncritical *Marine Shells of Port Alfred, South Africa* published by W H Turton in 1932 The need for an authoritative and comprehensive account of this most interestingly diverse fauna has long been clear This task has now been assumed by Brian Kensley of the South African Museum in a volume devoted to gastropods After an informative introduction, full scope is given to the work of a team of three artists who illustrate, often in colour and invariably with great clarity, all the 900 species

While I would have welcomed information about habits and habitat, certainty about species is the first essential and both professional and amateur malacologists will welcome this book and look forward to its successor covering the bivalves and other marine molluscs This is a South African Museum Publication but strangely carries no price nor any indication of the locality of the shore scene depicted on the end papers

C M. YONGE

Thermoelectricity

Thermoelectricity in Metals and Alloys By R D Barnard Pp x+259 (Taylor and Francis London, November 1972) £6 50

It is more than ten years since the late D K C MacDonald published a splendid monograph on thermoelectricity in metals and alloys Whilst there have not been any dramatic advances in the subject since then, a new monograph can certainly be justified on the grounds that the intervening period has been one of consolidation Our understanding of the thermoelectric power of metals is now in a very satisfactory state, in particular, at high temperatures, the dominating influence of the energy dependence of the scattering cross-section (rather than detailed consideration of Fermi surface topology) has led to a unified theory which covers solids, liquids and alloys Dr Barnard has covered the literature very adequately and his presentation of a mass of new material has ensured that the underlying unity of the subject has been preserved I was particularly impressed with chapters 4 and 6 which cover a whole range of high temperature effects from a standpoint based on electron scattering The remaining chapters cover the basic "classical" theory (chapters 1, 2 and 3), the ideas behind the concept of phonon-drag (chapter 5) and a general review of thermoelectricity in metals and alloys, particularly those in which the d-bands materially affect the experimental results

One criticism I should have liked to see a little on those cases where the basic formulation is beginning to break down, for example, low density Hg or alloys in which the mean free path is short This area of condensed matter physics is not well understood and a short account of some of the recent experiments would, I think, round the book off rather nicely

But, this minor point aside, I found Dr Barnard's book very readable and it will be useful to academic staff and research students who have to lecture on or research into thermoelectricity and its associated phenomena

J E. Enderby

Classic Ecobotany

Stålfelt's Plant Ecology: Plants, the Soil and Man. Translated by Margaret S Jarvis and Paul G Jarvis Pp x+592 (Longman London, December 1972) £5 50

This translation of the classic treatise on plant ecology by the late Professor Stålfelt, of Lund, has placed in the hands of British ecologists an introduction to an extensive continental literature on the subject In many respects Stålfelt was ahead of his time, for he anticipated the development of ecosystem theory and its application to agriculture, forestry and the maintenance of stability in the natural environment

The emphasis of the book is upon the interaction between plant and soil and it has a distinct bias towards the applied branches of ecology, which is rather refreshing when so many modern texts are exclusively theoretical

Although the translation reads well, it is sad that more recent work was not incorporated Of the seven hundred references in the bibliography, only about forty are later than 1960 As a reference text for undergraduate teaching it also suffers the disadvantage of being exclusively botanical when many introductory ecology courses are now integrated botany and zoology It will provide a useful introduction to plant ecology for undergraduate students of agricultural botany and forestry, although even in its coverage of these fields there is an evident neglect of biotic factors, for example competition and grazing One wonders whether the translators would have been more profitably employed in writing a new text based on Professor Stålfelt's work

Peter D Moore

African Avifauna

Birds of West Central and Western Africa By C W Mackworth-Praed and C H B Grant Volume 2 Pp vi+818+plates 47–93 (Longman London, April 1973) £8

The surviving author is to be congratulated on the completion of an ambitious project for covering the whole of Africa south of the Sahara with a uniform system of ornithological textbooks There are three series, each consisting of two volumes, and these deal respectively with eastern and northeastern Africa, with the southern third of Africa, and with west central and western Africa. There is of course some overlap of species but each series is complete in itself The first series opened in 1952 and ran into a second edition, the second appeared in 1962–63, and the earlier volume of this series came in 1970 Captain Grant died in 1958, but by then he had put in many years of preparatory study at the British Museum (Natural History) and had laid the foundations, especially as regards taxonomy, of the whole work, he is thus fittingly regarded as joint author even of this final volume.

The area covered by the third series is larger than that usually denoted by the term West Africa, and extends from southern Mauritania to northern Angola, as well as eastwards to the borders of the Sudan, Uganda and Tanzania. This second volume includes all the passerine families except the larks There are 736 species, some with several recognized races, and each of the latter receives separate treatment For each, as before, brief particulars are given of distinguishing characters, distribution (with marginal map), habits, nest and eggs, recorded breeding and call The colour plates figure every species except a few for which drawings have been considered sufficient

There are some excellent books, of various dates, on the birds of particular parts of Africa, and there are important recent works making a broad biological approach to the whole avifauna But as a systematic basis for study of the birds of the Ethiopian Region the six volumes of Mackworth-Praed and Grant have no equivalent

A Landsborough Thomson

Oxide Films

Oxides and Oxide Films Edited by John W Diggle Volume I Pp xiii+537 (Marcel Dekker New York, November 1972) $27 50

This book is the first of a series to be devoted to the general field of the anodic behaviour of materials The introduction by the editor shows the extent of the aim, which can fairly be described as electrochemical in its bias

There are to be four volumes on oxides and oxide films, each containing four lengthy reviews of particular topics The editor acknowledges that some reviews, peripheral to the main topic, will not be electrochemical and one may cite in this area for example "Dielectric Loss Mechanisms in Amorphous Solids" (to appear in volume 2) It does seem unfortunate that the editor has not thought it necessary to find a title of each volume which describes the contents more precisely The present one is not incorrect but which oxide films? The corrosion films on iron and steel, or the magnetic films used in computer memories, or what?

This first volume opens with an article by V Brusić on Passivation and Passivity in which passivation phenomena are discussed and the characteristics of the active and passive states are presented There follows M J Dignam's article on Ionic Transport Mechanisms through oxide films The various mechanisms by which the migration of a charged carrier can occur are studied and applied to chosen problems such as vitreous metal oxides C A Mead has contributed an article on Electronic Current Flow Through Ideal Dielectric Films, relating this to thermionic currents in diodes and in semiconducting and insulating films The final article, by S M Ahmed, is on the Electrical Double Layer at Metal Oxide-Solution Interfaces, presenting an extensive review of published work. Each article concludes with a very adequate list of references

This is clearly a book for the specialist, yet there are parts of each article from which the tyro can learn and profit But, as so often happens today, the price will probably restrict purchases to libraries and to committed research groups K J STANDLEY

Research on Whales

The Sperm Whale By A A Berzin Translated from Russian Pp v+394 (Israel Program for Scientific Information Jerusalem, Wiley Chichester, March 1973) £13 15

THE sperm whale is the most numerous of the great whales It contributes about 60% to the world catch of large whales, and nearly half are taken by the USSR It is also biologically fascinating because of its adaptations to the marine environment This dual interest led Dr Berzin to assemble his monograph of all the data available on the sperm whale up to 1968 The Soviet whaling fleets in the North Pacific and Antarctic and cruises by research vessels have provided much information which is not widely known to non-Russian scientists, so this critical review of published work and the author's original material is a competent and most welcome survey

Preferring the specific name *Physeter macrocephalus* L (1785), Berzin recognizes northern and southern hemisphere sub-species differing slightly in morphometry but not in colour He covers the osteology of the sperm whale, its digestive, respiratory and urinogenital systems, and with V M Malyshev, gives the first full account of the musculature Recent work on the brain is outlined, and the structure and possible functions of the skin are considered, including the questions of laminar flow and thermoregulation The curiously formed head of the sperm whale has long intrigued researchers, and recent evidence suggests functions of the nasal passages and spermaceti organ connected with sound production It is encouraging to find that Berzin states the theories but also expresses reservations where necessary on this and other unproven aspects of the whale's biology

Research on whales has tended to proceed in parallel in the Soviet Union and outside in recent years, perhaps because of the language problem This is particularly apparent in the discussion of reproduction and age determination For example, the author suggests that ovulation in the females is induced, foetal growth is not constant, lactation lasts only one year, and he gives important evidence for believing that two growth layers are formed in the tooth dentine each year Opinion elsewhere differs on these subjects, partly because the Soviet results published as long ago as 1961 have not been widely considered It is good to have a truly critical review of Soviet research available now, and this may help to avoid a repetition of the situation where the slow maturation of the sperm whale testis was described by Berzin in 1963 but recognized independently by other workers some five years later

Other subjects dealt with are behaviour, and diseases and parasites, including a thorough survey of the helminth fauna by S L Delyamure and A S Skryabin Food species, mainly cephalopods, may influence the distribution of sperm whales, and reference is made to the large body of relevant data accumulated in the USSR There is also an outline of sperm whale catches world-wide, with a useful account of Soviet whaling methods and products

Our knowledge of sperm whale biology, and reproduction in particular, has advanced since the last of the extensive references quoted was published, but otherwise this excellent translation gives a comprehensive picture of an important international resource

RAY GAMBELL

Light-Scattering

Light Scattering from Polymer Solutions Edited by M B Huglin Pp xviii+885 (Academic New York and London, August 1972) £14 50, $45

THE method of light-scattering has been applied to physical chemistry of macromolecules in solution owing to the works of P Debye in 1944 and has seen a successful development in the field of the polymers, synthetic as well as biological From this time the abundance of literature on this subject has shown the considerable interest of the method for the study of polymer solutions

There exist a number of reviews giving the main outlines of the theory and the various aspects of this method A few basic papers more specialized and already published in different journals have been reprinted in one volume in 1964 But the progress in the research of polymers makes necessary a more detailed and modern review on the information obtainable by this method Consequently the publication of a treatise entirely devoted to scattered light became indispensable This important book fulfils this purpose The wish of the editor is "to bridge the gap between the standard book and the papers of an extreme specialization" This new treatise on light-scattering is made up of eighteen chapters, each one, written by an expert, is self contained without reference to each other

The topics have been selected by the editor himself But no chapter is devoted to fundamental bases of the method, except one dealing with "large particle scattering function" P(θ) which is known to yield important information on the molecular geometry The essentials of theory are presented, more or less briefly, however, by most of the authors as an introduction to their own subject

In the beginning of the book, five chapters concern the technology The first one is devoted to the very important problem of clarifying the solutions In another chapter, the various apparatuses are described, but, unfortunately, the references being no later than 1966, recent improvements such as the use of laser as light source are hardly mentioned An important part (150 pages) is reserved for the determination of refractive index increments, which shows its importance, the tabulated data will be very useful for the experimenter

Among the following chapters treating various problems of polymer solutions, some concern both the synthetic and biological ones For example, chapter 9 deals with the problems of aggregation or multimerization, chapter 15 with the interactions between polymers and mixed-solvent and chapter 16 with the solutions of polyelectrolytes But most of them are devoted to synthetic polymers, stereoregular and copolymers It is worth noting particularly some topics which are untreated elsewhere, such as the influence of various external factors, pressure and temperature, or the effect of electric fields owing to which, beside the standard data, information on the dipolar moment, relaxation time and molecular flexibility is obtainable The last chapter deals with the early development of the turbidimetric titration, very useful in determining the molecular weight distribution

Although this book is devoted to "polymers" taken in the broadest sense, and so including biopolymers, the space given to biological topics, around fifty pages, permits only an incomplete view of the possibilities of the method in this field

The rapid survey of this important volume emphasizes the wealth of information brought by the light-scattering method But the detailed development of one subject in each chapter and the specialization of each one will make difficult the utilization of the book by anyone encountering the method for the first time Rather it is suited to polymer scientists, already experienced researchers, for whom it will be an invaluable tool

J TONNELAT
S GUINAND

CORRESPONDENCE

Mercury in Lakes

SIR,—Recently, Aston *et al*[1] reported that the mercury concentrations within a sediment core from an English lake were highest in the upper layers of sediment Others[2,3] have reported similar findings All have attributed this differential distribution in part to the possibility of increased inputs of mercury with time due to man's activities

Although there has been some discussion as to the source of this input[4,5], a lingering problem involves demonstrating that mercury levels in organisms have become generally elevated Several researchers[6-8] have compared mercury levels in old and recent biological samples and could not document a general increase of mercury content in life forms as time passed It may be, then, that mercury levels have always been highest in upper sediment layers

Aquatic organisms can concentrate mercury in their bodies When they die, sink, and decompose, they would add significant amounts of mercury to the upper sediments The life cycle of benthic insects offers a particularly striking pathway whereby mercury could be carried upward and ultimately deposited at the sediment-water interface There is some evidence that tubificid worms could carry substances upward in sediments[9] Some fish and algae are known to have high mercury loads Death and decomposition of these organisms would increase the mercury content of upper sediments In short, the activity and death of aquatic organisms would continually cycle mercury to the upper sediment layers

As others have mentioned[1,2], several researchers have proposed a geochemical mechanism whereby mercury diffuses upward in sediments This too may enhance the occurrence of elevated mercury levels in upper sediment layers

Except in sediments from known mercury contamination areas, the phenomenon that mercury concentrations tend to be highest in upper sediment layers may be a natural condition and not attributable to recent inputs of mercury

Yours faithfully,

C S SIKES
M P DRAIN

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Solar Energy

SIR,—The International Solar Energy Society was formed in 1954 to serve as a centre for information on research and development in the utilization of solar energy The Society headquarters are in Melbourne, Australia , in countries where sufficient interest exists, national sections of the Society have been established

At present, there is no British section, although there are nearly enough individual members to allow the formation of one If such a section were formed it would, by means of newsletters and meetings, bring together British scientists, engineers and environmentalists whose work involves the nature and use of solar energy

I am assessing the possibility of forming a British section I should be very grateful to receive any comments, or to send further details of the ISES to anyone who is interested

Yours faithfully,

M D ARCHER

The Royal Institution,
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Obituary

Dr Muriel Robertson

DR MURIEL ROBERTSON, FRS, who died on June 20 at the age of ninety, was educated at Glasgow University, where she graduated as an MA in 1905 and which subsequently awarded her a DSc and, in 1948, an LlD She spent three years as a Carnegie Research Fellow in Ceylon, studying various parasitic Protozoa in the blood of reptiles and fishes Thus she was introduced to the trypanosomes, a group on which much of her subsequent research was to be done She discovered and named a trypanosome of a turtle and studied its complete life cycle in both vertebrate and invertebrate hosts (leeches) This was one of the first life histories of a member of this genus to be elucidated in detail

Dr Robertson then returned to Britain in 1909 to work for a year as research assistant to Professor E A Minchin at the Lister Institute, and subsequently joined the Institute's staff No doubt it was from Professor Minchin that she acquired much of the cytological expertise she was later so fruitfully to apply to her studies of trypanosomes and other protozoa In 1911 her wanderlust reasserted itself, and she joined the Royal Society's Sleeping Sickness Commission in Uganda, under Dr H L Duke, as Protozoologist to the Uganda Protectorate Travel to such relatively unknown regions as central Africa was not commonly undertaken by young ladies in the early years of this century, and Dr Robertson's achievements in this field testify to her adventurous and determined nature, exemplified also perhaps by her use of a bicycle as a means of transport through the forests of southern Uganda

This period could perhaps be regarded as the acme of her scientific career, when she worked out in detail the entire, complicated developmental cycle undergone by *Trypanosoma gambiense*, the causative organism of human sleeping sickness, which was at that time devastating the population on the northern shore of Lake Victoria This work, published mainly in the *Proceedings* of the Royal Society, involved cytological studies of extreme delicacy and her beautifully illustrated papers are undoubted classics Her work on this subject has never been superseded nor indeed equalled, and the accuracy of some of her conclusions (for example, the role of the stumpy blood-stream trypomastigote in infecting the vector, *Glossina* spp) is only now being fully appreciated

After this period Dr Robertson returned to the Lister Institute in 1915 as protozoologist, a post which she occupied for the remainder of her working life, which continued until she was at least 78 During the First World War she showed her versatility by making valuable studies, eminently practical at that time, of the anaerobic bacteria causing gas gangrene, and she became secretary of the Medical Research Council's first Anaerobes Committee and a contributor to the Council's System of Bacteriology Later, she returned to her first scientific loves, the protozoa, continuing her elegant cytological studies on the free living flagellate *Bodo* and on the finer details of nuclear structure and division in *Trypanosoma* Miss Robertson's practical nature reasserted itself and she began a long series of pioneering studies of the host's immune response to the parasite *Trichomonas foetus*, an economically important cause of bovine abortion This work was summarized in her contribution to the book *Immunity to Protozoa*, published in 1963 when Miss Robertson was 80. She celebrated her 80th birthday by delivering the sixth Marjory Stephenson Memorial Lecture to the Society for General Microbiology, in which she discussed the cytology, life cycles and what she referred to as "the highly experimental approach . . to sex" of her beloved protozoa In this wide ranging review she showed a wholly typical grasp of modern techniques by referring to electron-microscope observations as well as to her own pioneering researches and to the work of many others, spanning the intervening half-century Her scientific achievements were recognized by her election to an FRS in 1947

Everyone who met Dr Robertson was impressed by her kindliness, her willingness to impart knowledge, her enthusiasm for her subject and her forthright personality She belonged to a generation of female scientific explorers which was probably unique Not only will she be sadly missed by her many friends and her wide circle of scientific acquaintances, but science as a whole will be the poorer for her death Happily, her great contributions to knowledge remain in the scientific literature and in the work of those whom she advised and inspired

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

Tate and Lyle Limited Group Research and Development—Annual Report for 1972 Pp 65 (Reading, Berks Tate and Lyle Limited, Group Research and Development, 1973) [105

University of Oxford Graduate Studies Students under Boards of Faculties and Committees as on the first day of Trinity Term 1973 Pp 227–335 (Oxford· The University, 1973) 10p [105

Department of the Environment. Water Pollution Research Technical Paper No 13 Mathematical and Hydraulic Modelling of Estuarine Pollution (Proceedings of a Symposium held at the Water Pollution Research Laboratory, 18th and 19th April, 1972) Pp vi+228 (London· HMSO, 1973.) £8 60 net [105

Report by the Hydrographer of the Navy 1972 Pp 38 (NP 130) (Taunton Hydrographic Department of the Ministry of Defence, 1973) [105

Shoe and Allied Trades Research Association Annual Report for 1972 Pp iv+173 (Kettering, Northants Shoe and Allied Trades Research Association, 1973) [155

BP Statistical Review of the World Oil Industry 1972 Pp 24 (London The British Petroleum Company, Ltd, 1973) [155

Psychiatrists in Training The Report of the Royal Medico-Psychological Association's Manpower and Education Project By Peter Book (*British Journal of Psychiatry*, Special Publication No 7) Pp xii+163 (Ashford, Kent Headley Brothers, Ltd, 1973 Published by authority of the Royal College of Psychiatrists) £2, $5 35 [155

Genetic Studies in Mental Subnormality By B C Clare Davison, Peter N Swift, Philip F Benson and John D Studdy (*British Journal of Psychiatry*, Special Publication No 8) Pp 82 (Ashford, Kent Headley Brothers, Ltd, 1973 Published by authority of the Royal College of Psychiatrists) £2, $5 35 [155

Natural Environment Research Council Institute of Geological Sciences Geomagnetic Bulletin No 4. Magnetic Results 1970 Eskdalemuir, Hartland and Lerwick Observatories Pp ix+154 (London: HMSO, 1973) £4 [155

Plastics and the Plastics Industry a Select Catalogue Pp 20 (London LINK Liaison Officer, Central Reference Library, Brixton Oval, SW2, 1973) *Gratis* [165

Department of Trade and Industry Production and Reserves of Oil and Gas on the United Kingdom Continental Shelf a Report to Parliament by the Minister for Industry Pp 12 (London HMSO 1973) 20p [165

The British Food Manufacturing Industries Research Association Annual Report 1972 Pp 54 (Leatherhead The British Food Manufacturing Industries Research Association, 1973) [165

Proceedings of the 12th NIAB Crop Conference, 13/15 December 1972 UK Cereal Production after entering the Common Market Pp 83 £1 List of Recommended Varieties 1973 Pp 8 (Cambridge National Institute of Agricultural Botany, 1973) [165

Science Research Council Daresbury Nuclear Physics Laboratory—Annual Report 1972 Pp 141. (Daresbury, Nr Warrington Daresbury Nuclear Physics Laboratory, 1973) [165

Countryside Commission for England and Wales Countryside Recreation Staff—a Paper for Discussion Pp 13 (London Countryside Commission, 1 Cambridge Gate, Regent's Park, NW1, 1973) *Gratis* [165

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CERN—European Organisation for Nuclear Research CERN—73-4 High Accuracy, Two-Dimensional Read-Out in Multiwire Proportional Chambers By G. Charpak and F Sauli Pp iii+10 (Geneva CERN, 1973) [23

World Health Organization Drug Therapy of Cancer By G Brule, S J Eckhardt, T C Hall and A Winkler Pp 163 20 Sw francs, £2, $5 Technical Report Series No 507 Psychogeriatrics—Report of a WHO Scientific Group. Pp 48 4 Sw francs, 40p, $1 (Geneva WHO· London. HMSO, 1972 and 1973) [23

US Department of Commerce National Bureau of Standards NBS Special Foreign Currency Program in Yugoslavia, 1971–72 By H Steffen Peiser Samuel F Chappell, Emanuel Horowitz, Harvey Yakowitz and Doris Blurbond (NBS Technical Note No 753) Pp v+65 (Washington, DC US Department of Commerce, National Bureau of Standards, 1973 For sale by US Government Printing Office) 90 cents [23

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Research in Biological Diversity

Editor D. Viza

Faculté de Médecine Pitié-Salpétrière, Pathologie Générale et Expérimentale
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APPOINTMENTS VACANT

AUSTRALIA

The New South Wales State Cancer Council

THE MEDICAL DIRECTOR

The Council is seeking a Medical Director of The New South Wales State Cancer Council He shall also be in charge of and responsible for the re-development of the Special Unit for research into human cancer

The Council has in mind the need for change in character of the Special Unit and for its possible re-development as an institute The nature of these changes will depend on the interests, qualifications and experience of the Medical Director and so the Council does not wish to lay down terms and conditions of appointment which are so explicit that they will restrict the Medical Director after his appointment

Therefore the Council, while outlining the qualifications, as stated hereunder, that it seeks in its Medical Director, is prepared to discuss appropriate variations of these with candidates

Council will welcome enquiries from interested persons who

(a) are medical graduates qualified for registration in New South Wales,
(b) are of clinical professorial status,
(c) have already had substantial experience in cancer research or have demonstrated their potential to direct and conduct such research
(d) will work full-time with the Council and will be responsible for the general administration of the Council and the Special Unit or Institute,
(e) wish to teach medical and science graduates and undergraduates and to supervise postgraduates

Further enquiries may be made of The Chairman of the New South Wales State Cancer Council, The Vice Chancellor, Sydney University, Sydney 2006 The closing date will be January 31, 1974 (267)

THE ROYAL SOCIETY

has vacancies for secretaries to assist in a wide field of activities concerned with assisting scientific research, exchange visits of scientists and education Interesting and responsible work in premises overlooking St James's Park Progressive salary scales, L V s, restaurant and pension scheme Telephone or write to Mr N Le Grand at 6 Carlton House Terrace, London SW1Y 5AG (01-839 5561) (449)

CSIRO

AUSTRALIA

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas The Organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia

DIVISION OF ENTOMOLOGY

RESEARCH SCIENTIST

FIELD: FUMIGATION INVESTIGATIONS

GENERAL: The Division is the main centre in Australia for basic research on insects, with a professional staff of over 100 The headquarters is at the Black Mountain Laboratories in Canberra, and there are important units in Queensland, New South Wales, Tasmania, Western Australia and overseas The Division is well equipped, its instrumentation including gas chromatography, N M R, mass spectrometry, and scanning and conventional electron microscopy Good library facilities are available also

The Division is establishing a grain storage unit in Canberra which will undertake studies of the biology, ecology, physiology and biochemistry of stored products, insects, mites and moulds and investigations into basic aspects of chemical and non-chemical means of pest control

DUTIES: The appointee will conduct research into the toxicity of fumigants to insect pests of grain In particular, he will study biological aspects of resistance to fumigants and develop methods of detecting such resistance in stored product Lepidoptera The work is to provide a background of information leading to the improvement of practical fumigation techniques

QUALIFICATIONS: A Ph D degree, or equivalent qualifications, with sound training in the biological sciences and good chemical expertise, and demonstrable research ability

SALARY: The appointment will be made within the ranges of Research Scientist or Senior Research Scientist $A8,489-$A12,932 p a

TENURE: Either a fixed term or an indefinite appointment may be negotiated An indefinite appointment carries Commonwealth Superannuation benefits

Applications stating full personal and professional details, the names of at least two professional referees, and quoting reference number 180/674, should reach —

The Personnel Officer,
Australian Scientific Liaison Office,
64-78, Kingsway, London, WC2B 6BD

by the 21st September, 1973

Applications in U S A and Canada should be sent to —
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N W,
Washington, D C 20036, U S A

(403)

(RE-ADVERTISEMENT)

PORTSMOUTH POLYTECHNIC

DEPARTMENT OF CHEMISTRY

RESEARCH ASSISTANTS

Vacancies will arise shortly for research assistants to work in inorganic, organic and physical chemistry Applicants for these posts must possess an honours degree, or a Grad R I C or an equivalent qualification involving chemistry

Salary scale £1,120×£50 to £1,220 per annum (under review)

Research Assistants are expected to work for a higher degree and are encouraged to publish their results

The preferred areas of study are

(1) Catalytic oxidation of hydrocarbons
(2) Factors affecting the triboelectric separation of mineral particles
(3) Froth flotation of minerals and correlation with adsorption from solution of conditioning agents
(4) Microbiological transformations of compounds of medical interest
(5) Enzyme kinetics

Application forms may be obtained from the Staff Officer, Portsmouth Polytechnic Alexandra House, Alexandra Road, Portsmouth PO1 2QQ, to whom completed applications should be returned as soon as possible Please specify interest and quote ref D43 Previous applicants need not re-apply (380)

FLINDERS UNIVERSITY OF SOUTH AUSTRALIA

LECTURER IN BIOLOGY

(ECOLOGY)

Applications are invited for appointment to the above-mentioned position in the School of Biological Sciences

The School is a fully integrated School, without separate departments, and with teaching and research interests extending broadly into the fields of biochemistry, biophysics, developmental biology, genetics, microbiology, physiology, behaviour and taxonomy

The School wishes to expand its interests in the area of Community Biology, and invites enquiries from suitably qualified candidates Preference may be given to an applicant with broad interests in ecology

Informal enquiries concerning the School may be addressed to the Chairman, Dr B A Barlow, in the University

Salary scale $A8,698-$A11,982 Superannuation is on the FSSU basis

Further information about the position, including conditions of appointment and details required of aplicants, may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts) 36 Gordon Square, London WC1H 0PF Applications should be lodged with the Registrar, The Flinders University of South Australia, Bedford Park, South Australia, 5042, not later than September 17, 1973 (396)

Overseas Development Administration
Land Resources Division, Surbiton, Surrey

Irrigation Engineer/ Hydrologist

■ **Appraise and plan use of water resources in developing countries ■ Investigate hydrological cycle ■ Prepare outline designs of irrigation schemes employing surface or sprinkler systems ■ Considerable periods overseas.**

□ Degree or equivalent in Civil or Agricultural Engineering □ Postgraduate training or experience in irrigation engineering and water use, preferably in developing countries □ Age normally under 32 □ Appointment as Scientific Officer (£1408–£2267), Higher Scientific Officer (£2166–£2757) or Senior Scientific Officer (£2705–£3730) according to age, qualifications and experience □ Ref SA/2/JB □ Closing date 14 September 1973

□ Application forms from the Establishment Officer, Land Resources Division, Overseas Development Administration, 8th Floor, Tolworth Tower, Surbiton, Surrey

Procurement Executive, Ministry of Defence
Microbiological Research Establishment,
Porton Down

Senior Research Fellow - Virology

■ **Study differences in virulence between serologically indistinguishable strains of virus ■ Investigate cellular and humoral responses to infections, particularly respiratory infections with arthropod borne viruses ■ Full range of supporting services available.**

□ Good honours degree in appropriate subject □ At least 3 years' postgraduate experience in virology, preferably in medical virology □ Appointment, for 3 years, as Senior Research Fellow □ Salary range £2460–£3100, according to qualifications and experience □ Ref SC/2/FQ □ Closing date 14 September 1973

□ Application forms from Mr R Mills, Procurement Executive, Ministry of Defence, Room 302, Savoy Hill House, Savoy Hill, London WC2R OBX

British Museum (Natural History)
Department of Entomology

Entomologists

■ **2 posts ■ Taxonomic and zoogeographic research on Diptera Cyclorrhapha or Microlepidoptera ■ Curatorial work on relevant National Collection ■ Opportunities to collect abroad.**

□ 1st or 2nd honours degree in Zoology, preferably with Entomology □ At least 2 years' postgraduate research experience □ Age under 32 □ Appointment as Higher Scientific Officer (£2251–£2842) or Senior Scientific Officer (£2790–£3815), according to age and experience □ Ref SB/8/DK □ Closing date 7 September 1973

□ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service)

Forestry Commission
Alice Holt Lodge, Farnham, Surrey

Entomologist

■ **Develop methods of assessing forest insect populations for production of simple models of host/insect systems ■ Collaborate in data handling and analysis ■ Investigate methods of injecting systematic insecticides into trees.**

□ 1st or 2nd class honours degree in Zoology (Entomology), Applied Entomology or Biology □ Working knowledge of statistical techniques and simple population modelling desirable □ Age under 30 □ Appointment as Scientific Officer (£1,318–£2,177) or Higher Scientific Officer (£2,076–£2,667), depending on qualifications and experience □ Promotion prospects □ Ref SA/3/DM □ Closing date 14 September 1973

Soils Chemist

■ **Study (in forest and laboratory) the soils factors controlling the growth of trees and their response to added fertilisers.**

□ 1st or 2nd honours degree in Chemistry, an earth or plant science, or Forestry experience, particularly in field trials and investigations □ Some experience of chemical analysis □ Knowledge of biology would be an advantage □ Age under 32 □ Appointment will be as Higher Scientific Officer (£2076–£2667) or Senior Scientific Officer (£2615–£3640) depending on qualifications and experience □ Ref SA/2/DM

□ Closing date 14 September 1973

□ Application forms from the Personnel Officer, Forestry Commission, Priestley Road, Basingstoke, Hants

Science group
CIVIL SERVICE

(426)

INSTITUTE OF UROLOGY

(University of London)
in association with St Peter's Hospitals

Applications are invited for a RESEARCH FELLOW (with medical and/or scientific qualifications), in the grade of Lecturer (Senior Registrar status) for an investigation into the ultrastructure of the kidney and urinary tract epithelium The successful applicant will be attached to the Electronmicroscopy Unit in the Department of Pathology, St Paul's Hospital Appointment for one year in the first instance subject to renewal

Applications to the Pathologist, St Paul's Hospital, Endell Street, London W C 2 (342)

PhD IN ANIMAL ECOLOGY

Freshwater or terrestrial Animal Ecologist to be appointed, beginning September 1973, at the Assistant Professor level Salary $11 000 to $12,000, depending upon experience Responsibilities include participation in the undergraduate curriculum and development at a teaching-research specialization at the PhD level Minority applicants invited

Send curriculum vitae, the names of three referees, and a statement of teaching interests and research plans to Chairman, Department of Zoology and Microbiology Ohio University, Athens, Ohio 45701 Ohio University is an equal opportunity, affirmative action employer (393)

TECHNICAL OFFICER

required for a new development in ultrasonic honography as related to the eye Applicants will be graduates, with physics as the main subject Experience in electronics and an interest in ultrasonics desirable This post will be vacant from October 2, 1973, and offers scope for original research and the application of this technique to ophthalmic problems Salary in the range £1,947-£2,469 per annum, plus £126 London Allowance

Applications in writing by September 14, 1973, with full details of qualifications and experience, to The Secretary, Institute of Ophthalmology Judd Street, London WC1H 9QS, quoting reference 131/61 (408)

CSIRO

AUSTRALIA

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas The Organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia

DIVISION OF ENTOMOLOGY

ENTOMOLOGIST/ECOLOGIST

GENERAL: The Division is the main centre in Australia for basic research on insects Its headquarters is located in Canberra, A C T , and it maintains laboratories elsewhere in Australia and in a number of overseas countries, including South Africa Currently eight staff are stationed there in a programme concerned with selecting dung beetles for establishment in Australia to prevent pasture pollution and to control dung breeding fly pests

The headquarters of the successful applicant will be in the Division's laboratory in *Pretoria*

DUTIES: Under the general supervision of the research leader, to participate for part of each year in expeditions in Africa and elsewhere for the purpose of studying and selecting dung beetles, to set up stocks of selected species in the insectaries in Pretoria, to supervise the study and the propagation of the cultures, and to assist the research leader to co-ordinate the general activities of the laboratory

QUALIFICATIONS: An honours degree in science, with a major in the biological sciences Some postgraduate experience is essential, preferably in entomology or field ecology Applicants should be of good physical build, with a liking for outdoor work, and a tolerance for hot and humid conditions, likely to be encountered in field work

CLASSIFICATION. Senior Scientific Officer—Rand 5520–Rand 6210 p a

CONDITIONS: The successful applicant will be attached to the staff of the Australian Embassy, Pretoria The initial anticipated tenure is four years but this could be extended However, after an initial period of at least one year, the appointee may be eligible for appointment to the staff of CSIRO

The Organization will bear the cost of transferring the appointee and family to Pretoria

Applications stating full personal and professional details, the names of at least two professional referees, and quoting reference number 180/681, should reach —

The Personnel Officer,
Australian Scientific Liaison Office,
64–78, Kingsway,
London WC2B 6BD

OR

The Chief,
Division of Entomology, CSIRO,
P.O. Box 1700,
Canberra City,
A.C.T., Australia, 2601

by the 21st September, 1973

Applications in U S A and Canada should be sent to —

The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N W ,
Washington, D C 20036, U S A

(411)

ROTHAMSTED EXPERIMENTAL STATION

STATISTICIAN to advise on the design and planning of livestock investigations to be done on Experimental Husbandry Farms of the Agricultural Development and Advisory Service, to supervise analysis of experimental results and help with their interpretation The Station has a computer with relevant suite of programs

Qualification First or good Second Class Honours Degree in mathematics or statistics, preferably with some knowledge of animal husbandry, physiology or nutrition , or a similar degree in a relevant biological subject with subsidiary qualifications in experimental statistics

Appointment in grade of Scientific Officer (£1,590-£2,177) or Higher Scientific Officer (£2,076-£2,667) according to experience Exceptionally, for a candidate with more than four years' relevant experience, appointment may be in the Senior Scientific Officer grade £2 615-£3,640) FSSU with allowance to offset contributions

Apply by September 24, 1973, giving names and addresses of two referees, and quoting reference 189, to The Secretary, Rothamsted Experimental Station, Harpenden, Herts AL5 2JQ (391)

UNIVERSITY OF SYDNEY

SENIOR LECTURESHIP/ LECTURESHIP IN PHYSIOLOGY

The person appointed will be required to take special responsibility in the teaching of Physiology to dental students , qualifications in dentistry would therefore be an advantage Research and teaching experience in cardiovascular and/or respiratory physiology would also be desirable

The position advertised is permanent but in appropriate cases an initial three-year appointment may be made with possibility thereafter of permanency or in certain cases return fares

Salary ranges Senior Lecturer—$A12,268-$14 308 . Lecturer—$A8,689-$11,982

Applications, including curriculum vitae, list of publications and names of three referees by September 28, 1973, to the Registrar, University of Sydney, N S W , Australia 2006, from whom further information available Information about conditions of appointment and application procedure available from Association of Commonwealth Universities (Appts) 36 Gordon Square, London WC1H 0PF (435)

THE POLYTECHNIC OF NORTH LONDON

Holloway, London N7 8DB

SRC RESEARCH TECHNICIAN

required from October 1, 1973, for three years to assist with a research team working on the cytology of gastropod molluscs

Write, giving full details of experience, qualifications and referees, to Dr C. R. Bantock, Biology and Geology Department, The Polytechnic of North London, Holloway, N7 8DB. (363)

FLINDERS UNIVERSITY OF SOUTH AUSTRALIA

SCHOOL OF MEDICINE

Applications are invited for the first NINE posts of SENIOR LECTURERS and LECTURERS in the Section of HUMAN BIOLOGY of the SCHOOL OF MEDICINE The Section of Human Biology comprises the fields of CLINICAL BIOCHEMISTRY, MORPHOLOGY, and PHYSIOLOGY It is envisaged that three initial appointments will be made in each of these fields The first stage buildings for this new school, which will be integrated under one roof with its 700 bed teaching hospital on campus as the FLINDFRS MEDICAL CENTRE, will be ready in July, 1974 A highly integrated undergraduate medical curriculum is planned and the first 64 medical students will enter the Centre in March 1975 In addition, postgraduate degrees in the medical sciences will be offered

The following professors have been appointed and are available for consultation

PROFESSOR G J FRAFNKEL, Chairman and Dean, School of Medicine, The Flinders University of South Australia Bedford Park, South Australia, 5042, Australia

PROFESSOR M N BERRY will take up his appointment as Professor of Clinical Biochemistry in January, 1974 Clinical Biochemistry will provide the biochemical diagnostic services for the Centre and research activities will include both basic and clinical investigation of the regulation of metabolism in health and disease In particular the relationships between cell structure and function, the metabolic derangements of diabetes mellitus and the biochemistry of alcohol and other drugs will be studied Address Department of Pathology and Cardiovascular Research Institute, University of California Medical Center, San Francisco California 94122, USA

PROFESSOR L B GEFFEN has already taken up his appointment as Professor of Human Physiology and is establishing facilities for research into basic aspects of chemical transmission in the nervous system In particular, biochemical, histochemical and immuno-chemical studies of catecholamines and their role in various disorders are being undertaken

PROFESSOR A W ROGERS will take up his appointment as Professor of Human Morphology in November 1973 In the discipline of Morphology, research will involve all aspects of communication between cells advanced equipment will be available for auto-radiography, morphometry and electron microscopy Address Department of Human Anatomy, University of Oxford, South Parks Road, Oxford OX1 3QX

Present salary scales are Senior Lecturer $A12,268-$A14,308 , Lecturer $A8,698-$A11,982

Appointees will be expected to take up their posts in July, 1974

Further information may be obtained from The Registrar, The Flinders University of South Australia, Bedford Park South Australia 5042, Australia, whom applications should reach by October 1, 1973 (395)

UNIVERSITY OF DAR ES SALAAM

TANZANIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN MATHEMATICS Applicants should have a Ph D or equivalent and/or considerable teaching experience at University level in some area of, Applied Mathematics Preference will be given to those specialising in Mechanics or Engineering Mathematics Salary scales (a) T£2,380-T£2,800 per annum (b) T£1,898-T£2,318 per annum (T£1=£1 16 Sterling) The British Government may supplement salary in range £550-£950 per annum (Sterling) for married appointee or £300-£650 per annum (Sterling) for single appointee (normally free of all tax) and provide children's education alowances and holiday visit passages FSSU Family passages biennial overseas leave

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail, not later than September 24, 1973, to the Chief Academic Officer, University of Dar es Salaam, P O Box 35091, Dar es Salaam, Tanzania Applicants resident in UK should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road London W1P 0DT Further particulars may be obtained from either address (422)

Organon International BV

Organon, a large Dutch international company manufacturing a wide range of pharmaceutical products, requires for the expanding activities of its Section of Reproductive Toxicology a

Zoologist/Biologist

The Section of Reproductive Toxicology and the Section of General Toxicology form the Department of Drug Safety This Department is responsible for administering programmes to evaluate the safety of drugs

The section of Reproductive Toxicology is concerned with the detection of undesirable side-effects of compounds on the reproductive processes (fertility, teratology, postnatology) with the help of animal experiments (mouse, rat, rabbit)

Applicants for this appointment should ideally be in the 20-30 age group and must possess a B Sc or an Honours Degree in one of the biological sciences (anatomy, embryology, physiology)

Research experience in one of these fields would be of advantage Within the company it is a rule that experimental results presented in subject reports are written in the English language

The salary will be competitive Assistance with housing will be given. Applications in the first instance should be forwarded to Personnel Department Organon, Kloosterstraat 6, Oss, the Netherlands

Organon

Organon International BV

(438)

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The Boots Company Limited, Nottingham, NG2 3AA

(415)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS AL5 2JQ

BIOLOGIST to work for one year on the effects of competition on phosphate uptake by mycorrhiza supported by an I B P grant Minimum qualifications are a degree, HNC or equivalent in horticulture, agricultural chemistry, soil science or botany with interest in ecology Salary up to £1,499 according to qualifications

Applications, with names of two referees and quoting reference 1932, to the Secretary by September 18, 1973 (392)

UNIVERSITY OF DAR ES SALAAM

TANZANIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN AGRICULTURAL EXTENSION/RURAL SOCIOLOGY Applicants should hold a good honours degree in Agricultural Economics with majors in Agricultural Extension/Rural Sociology or a B Sc (Agric) with post-graduate training in Extension and Rural Sociology Appointee will be expected to teach and conduct tutorial and field practicals to undergraduates in the fields of Agricultural Extension and Rural Sociology He will also be expected to undertake research in his teaching fields Salary scales (a) T£2,380-T£2,800 per annum (b) T£1,898-T£2,318 per annum (T£1=£1 16 Sterling) The British Government may supplement salary in range £550-£950 per annum (sterling) for married appointee or £300-£650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages FSSU Family passages , biennial overseas leave

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail, not later than September 24, 1973, to the Chief Academic Officer, University of Dar es Salaam, P O Box 35091, Dar es Salaam, Tanzania Applicants resident in UK should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London, W1P 0TD Further particulars may be obtained from either address (421)

CYTOGENETICIST/ KARYOLOGIST

Pfizer Limited, part of a large international organization prominent in Pharmaceuticals, Veterinary Products and Fine Chemicals, manufacture Oral Polio Vaccine in human diploid cells (WI 38) at their Sandwich plant in East Kent

The Vaccine Quality Control Department, as part of their control procedures, perform a number of chromosomal analyses on each batch of cells used

A Cytogeneticist or Karyologist is required to participate in this work and to lead the team of three technicians Experience in chromosomal preparation techniques and karyotyping (not necessarily human) is considered more important than formal qualifications, but this post would be suitable for a young graduate

The Company's conditions of service, fringe benefits and general amenities are good The Sandwich plant is in a rural setting close to the sea

Persons with requisite experience are invited to write for an application form to

Pfizer

J. E. T. Haile, Personnel Department,
PFIZER LTD.,
Sandwich, Kent.

(424)

Government of Malawi

Ministry of Agriculture and Natural Resources

require

Agricultural Research Officer

Salary up to £3,534 + tax free gratuity

Maximum emoluments equivalent to a U K salary of £5,000

To carry out research work in Irrigated Agriculture in the lowland areas of Malawi If sufficiently senior and experienced he will become the co-ordinator of all irrigated research work

Candidates, aged up to 50, must have a B Sc in Agriculture or equivalent with special qualifications or experience in the agronomy of irrigated crops

Paid leave with free passages and baggage allowance Education allowances and subsidised housing Loan for the purchase of a car Free medical attention

Please apply to MALAWI BUYING AND TRADE AGENTS, Recruitment Section, Abbey House, 6 Victoria Street, London, SW1H OLA for application form and further particulars quoting reference number 654/A.

(398)

UNIVERSITY OF BRISTOL

DEPARTMENT OF PATHOLOGY

A vacancy exists for a

RESEARCH TECHNICIAN

having HNC or equivalent qualifications plus several years' relevant experience, to take charge of a new electron microscope unit , experience in cell biology is desirable The work will involve also the use of sophisticated electron and optical equipment in connection with studies on brain damage, investigations on tissue culture and a general supervisory responsibility for the running of a small new laboratory

This "funded post" which is tenable at the Veterinary School, Langford, carries a salary related to UCGS scale grade 5 (£1,881 × £72 to £2,241 per annum—revision from October 1973 under review) , the present grant is annually renewable to December 1977 initially

Applications in writing, giving the names and addresses of two referees, to Professor I A Silver, Department of Pathology, Medical School University Walk, Bristol BS8 1TD

(368)

NATIONAL COUNCIL FOR SCIENTIFIC RESEARCH

Applications are invited from suitably qualified persons for the post of

BIOMETRICIAN

Applicants must have postgraduate degree or experience in mathematics or statistics with considerable research experience in sampling and experimentation Experience in sample survey techniques, and biometrics research is desirable

The Unit is primarily a consulting group and collaborates with various research units of the Council in fields such as animal productivity, forestry and insect ecology It also advises and assists organisations outside the Council on statistical problems

Salary according to qualifications and experience on the salary scales indicated below but a higher salary would be offered to exceptionally well-qualified and experienced senior scientists

Professional Officers	K3,240×240—K4,440
Senior Professional Officers	K4,680×240—K5,640
Principal Professional Officers	K5,840×240—K6,800

For Zambians there is a superannuation scheme Non-Zambians will be paid a gratuity of 25% of aggregate basic salary earned during service of not less than thirty months

Accommodation will be provided on an economic rental basis but not exceeding 10% of basic salary Hard furniture will be provided For non-Zambians travel and education allowances are available for minor dependent children attending school outside Zambia

Applications, giving full personal details qualifications, experience and naming three referees, should be submitted to The Secretary-General, National Council for Scientific Research, P O Box CH 158, Chelston Lusaka Zambia

(383)

QUEEN MARY COLLEGE

(University of London)

DEPARTMENT OF ZOOLOGY AND COMPARATIVE PHYSIOLOGY

Applications are invited for the post of RESEARCH TECHNICIAN (grade 3) to work in the field of insect neurophysiology on a project involving the structural and functional organisation of neural pathways in insect photoreceptors Applicants should have some knowledge of electrophysiological techniques and/or histology and fluorescence microscopy The appointment will be for approximately two years Salary £1,539 per annum plus London Weighting £175 per annum Five day week, five weeks (in total) annual leave

Letters only to Assistant Secretary (Establishment) (N), Queen Mary College, Mile End Road London E1 4NS, stating age, experience, qualifications and present work Closing date August 31

(336)

QUEEN'S UNIVERSITY OF BELFAST

CHAIR OF CANCER STUDIES

Applications are invited for a new Chair of Cancer Studies (joint appointment with the Northern Ireland Hospital Authority or its successor) from the earliest date that may be arranged Applications should be received by October 15, 1973

Further particulars may be obtained from the Personnel Officer, The Queen's University of Belfast BT7 1NN, Northern Ireland (Please quote Ref 73/N)

(371)

unilever research

Physiologist/Biochemist for Farm Animal Feeds Systems Research

You should be a Ph D, preferably with research experience in avian physiology and an interest in the physiological and biochemical aspects of food and water intake You will work in a small team of scientists developing new feeding systems for the fowl, and advise Unilever animal feed companies (e g , BOCM Silcock Ltd) on technical matters to incorporate research developments into their products

The Unilever Research Laboratory is the largest food research centre in Europe, with over 1,200 staff operating on two rural sites This vacancy is at Colworth House, a pleasant country estate 9 miles north of Bedford, in the Metabolic Section directed by Prof E F Annison Comprehensive modern facilities are available, and encouragement given to publish

Starting salary will be based on age and merit, in the range £2,100 (new Ph D) to £4,000 There are opportunities for promotion both in Research and in the wider field of Unilever Operating Companies (over 500, world-wide) Assistance with removal expenses and house purchase is available

Please write for further details and an application form to

The Personnel Officer (CWM 97/N),
Unilever Research Colworth/Welwyn Laboratory,
Colworth House, Sharnbrook, Bedford

(443)

LINTAS 732012562

Imperial
Chemical
Industries
Limited

Industrial Hygiene Research Laboratories

Ultrastructural Research

The Industrial Hygiene Research Laboratories situated at Alderley Park, near Macclesfield, Cheshire act as the Company's centre for toxicological advice and research The Experimental Pathology Unit of the Laboratories carries out ultrastructural and enzyme histochemical studies on the effects of chemicals on mammalian cells and organs A new post has been created for a person with a doctorate, preferably with experience in the application of electron microscopy to toxicological problems, who will be involved primarily in studies on the effects and mode of action of chemical carcinogens

Please write or telephone for an application form to

Mrs P M E Baker
Personnel Officer
Imperial Chemical Industries Limited
Fulshaw Hall, Wilmslow
Cheshire
Tel Alderley Edge 2828 ext 5358

(387)

UNIVERSITY COLLEGE, CORK

Applications are invited for the following appointments tenable from October 1, 1973

1 EXPERIMENTAL OFFICER

Qualifications Previous experience in the application of analytical techniques to food and/or extensive experience in gas chromatography

Duties To work with personnel in the departments of Chemistry and Dairy and Food Chemistry in the application of analytical methods for estimating nitrosamines and related species in nitrite-treated foods

Stipend and Duration £1,613 for 12 months (renewable for a second 12-month period)

2 SENIOR DEMONSTRATOR IN PHYSICAL CHEMISTRY

Qualifications M Sc or Ph D in physical chemistry

Duties Supervision of undergraduate practical courses in physical chemistry together with related tutorials and experimental work

Stipend and Duration £1,602 for 12 months (plus possible additional payments for research work supported by external funds)

Applications should be sent to J Cunningham, Professor of Physical Chemistry, to arrive before September 15, 1973 (439)

CSIRO

AUSTRALIA

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas The Organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia

DIVISION OF PROTEIN CHEMISTRY

POSTDOCTORAL FELLOW IN PROTEIN CHEMISTRY

The Division of Protein Chemistry is located at Parkville, Victoria, and has a research staff of some sixty organic and physical chemists, biochemists and biophysicists Research within the Division deals mainly with the structure and chemistry of the wool fibre and its constituent and related proteins, with the photochemical degradation of proteins, and with the development of new dyes and fluorescent whitening agents for use on wool It also includes studies on leather manufacture and on muscle proteins, seed proteins, enzymes and antigens

DUTIES. It is proposed to appoint a Postdoctoral Fellow to the Division for a period of three years to investigate the chemistry of the deposition of polymers on and within wool fibres There is need for a better understanding of the interaction of polymers and keratin and initially the successful applicant will be requested to devote special attention to the interaction of certain modified proteins with keratin

QUALIFICATIONS A Ph D degree in an appropriate field such as physical biochemistry, biochemistry or chemistry or equivalent qualifications, and demonstrable research ability

SALARY. The appointment will be made within the ranges of Research Scientist or Senior Research Scientist $A8,489–$A12,932 p a

Applications stating full personal and professional details, the names of at least two professional referees, and quoting reference number 462/388, should reach —

The Personnel Officer,
Australian Scientific Liaison Office,
64-78, Kingsway, LONDON, WC2B 6BD.
by the 21st September, 1973

Applications in U S A and Canada should be sent to —
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N W ,
Washington, D C 20036, U S A

(405)

Tissue Culture

A Research Assistant is required to assist in a programme of work involving cell culture and the isolation of products Applicants should hold an HNC or similar level biological qualification Practical experience in tissue culture and biochemistry would be an advantage (Ref BP 169)

This vacancy offers an opportunity to enter a company offering progressive salaries with excellent conditions of employment Encouragment will be given to the successful applicant to obtain further qualifications

There are excellent recreational facilities, staff restaurants and free company transport from Dorking station to Brockham Park

Please reply quoting reference to

Personnel Officer,
Beecham Research Laboratories,
Brockham Park, Betchworth, Surrey
Tel Betchworth 3202

1972

(417)

AN BORD SEIRBHISE FUILAISTRIUCHAIN
THE BLOOD TRANSFUSION SERVICE BOARD

BIOCHEMIST

Applications are invited for appointment to the whole-time post of Biochemist (Basic Grade) The person appointed will preferably be an honours graduate in Biochemistry or have an equivalent qualification and will be required to work in the Protein Fractionation Unit Interest in research and development work and experience of protein chemistry will be an advantage The Salary Scale will be £1,552 by £52(2) by £119(1) by £84(9) to £2,531 per annum, the point of entry being determined by qualifications and experience There is a contributory pension scheme in operation

Applications, stating age, qualifications, experience and the names of two referees, should be submitted to the Medical Director, Pelican House, P O Box 97, 52 Lower Leeson Street, Dublin 2, not later than August 31, 1973

(444)

BRISTOL POLYTECHNIC

POST-DOCTORAL RESEARCH ASSISTANT

(S R C Award)

A chemist is required to assist in the synthesis of a model for the Haem pocket in Haemoglobin This will involve both heterocyclic and peptide chemistry and will latterly entail the use of vacuum line techniques

The appointment will be for one year only at a salary of £1,788 per annum Opportunities for gaining high level teaching experience are available

Apply by letter, quoting names of two referees and career details, to Dr C L Honeybourne, Department of Science, Bristol Polytechnic, Ashley Down, Bristol BS7 9BU (437)

NATIONAL COLLECTION OF TYPE CULTURES

SCIENCE GRADUATE

at least 2 1, in a biological subject, preferably in microbiology This post includes care and maintenance of the bacterial strains in the Collection Over 3,000 strains of more than 300 species of medical and veterinary interests are kept, and provide a wide experience in systematic bacteriology These strains are maintained in a freeze-dried state and are regularly checked for their viability and characteristics Opportunities for the study of given groups and certain aspects of microbial classification are available A project is in preparation for data processing the laboratory records of the Collection

The NCTC has a Curator, Dr S P Lapage Deputy Curator, Mr L R Hill and three other graduate staff in addition, an affiliated project includes three graduate staff

Starting salary dependent on qualifications and experience from minimum of £1,566 plus £126 London Weighting per annum National Health terms and conditions of service and superannuation

Applications to Personnel Officer, Central Public Health Laboratory, Colindale Avenue, London NW9 5HT (402)

UNIVERSITY OF BIRMINGHAM

INSTITUTE OF CHILD HEALTH

A vacancy will be available from November 1, 1973, in a research unit investigating the biochemical defect in Cystic Fibrosis Previous experience with cell culture, cell separation methods or cell biochemical techniques an advantage

Salary range up to £1,671 per annum, under review from October 1, 1973

Reference 854/B/834

Applications with full details to Assistant Secretary (Personnel), University of Birmingham, P O Box 363 Birmingham B25 2TT (382)

FANCY A CHANGE

We have vacancies galore at every grade in the scientific field, including marketing

For further details, write or telephone
WALBROOK APPOINTMENTS,
116 HIGH HOLBORN, LONDON, W C 2
Tel 01-405 8787

(3)

UNIVERSITY OF EDINBURGH

DEPARTMENT OF BOTANY

RESEARCH ASSISTANTSHIP

Applications are invited for an ARC Research Assistantship to study the growth, morphogenesis and histochemistry of the shoot apex during flower development Applicants should have a good honours degree in a Biological or related subject

The successful applicant may register for a higher degree Remuneration will be at the same level as an SRC studentship

Applicants should write, giving the names of two referees, or telephone (031-667 1081, Ext 3319), as soon as possible to Dr R F Lyndon, Department of Botany, Mayfield Road, Edinburgh EH9 3JH Please quote reference 5062 (412)

THE ANIMAL VIRUS RESEARCH INSTITUTE

Pirbright, Woking Surrey

DEPARTMENT OF EXPERIMENTAL PATHOLOGY

Applications are invited for a post in the above Department Applicants should have had experience in histological histochemical and immunohistological procedures to provide support for a small group studying the pathogenesis of vesicular diseases in farm animals Familiarity with the preparation of specimens for, and the use of the electron microscope an advantage The appointment will be in either the S O grade (£1,318-£2,177) or H S O grade (£2 076-£2,667) depending on qualifications and experience Minimum qualifications required, degree in scientific subject I M L T H N C , H N D or equivalent for appointment in S O grade similar qualifications required for appointment in H S O grade with at least five years' appropriate scientific experience since qualifying applicants with first or second class honours degrees or equivalent should have had at least two years' postgraduate research experience Superannuation Scheme with allowance to offset contributions House available for suitable married applicant

Further particulars and application forms from Secretary (308)

UNIVERSITY OF OXFORD

DEPARTMENT OF GEOLOGY AND MINERALOGY

A TECHNICIAN Grade 5 (£1,881-£2,241) is required immediately in our Chemical Laboratories Minimum qualifications, A level Chemistry or ONC and experience in working in a Chemical Laboratory The Technician will be responsible for the day-to-day running of the Laboratories under the direction of a D R A He (she) will be primarily engaged in silicate analysis using modern apparatus and should be capable of instructing research students

Application should be made, giving the names of 2 referees to the Administrator Department of Geology and Mineralogy Parks Road, Oxford (416)

ELECTRON MICROSCOPIST required in Plant Science Laboratories, University of Reading, to assist in operation and maintenance of scanning and transmission electron microscopes Extensive practical experience necessary in electron microscopy and preparative techniques Applicants should have relevant HNC, HND, or Degree Salary in scale £1,881×£72—£2,241 per annum (Technician Grade 5)—Apply in writing, quoting Ref TN44, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH (378)

THE LONDON HOSPITAL
(Whitechapel)

GRADUATE RESEARCH ASSISTANTS OR QUALIFIED TECHNICIAN

Required in the professional surgical Research Unit

The work will be concerned with radio-immuno-assay and experience is necessary for only one of the posts

Applications to The House Governor, The London Hospital (Whitechapel), Whitechapel, London E1 1BB Tel 01-247 5454, Extn 388

Please quote Ref 189 (433)

Opportunity Overseas

This appointment is wholly financed by the British Government under Britain's programme of aid to the developing countries

Sierra Leone

FISHERIES ADVISER

Required to advise and assist with the overall planning and development of a team working with the Ministry of Agriculture and Natural Resources in Freetown Applicants who should normally be citizens of, and permanently resident in, the U K. should have a degree in Natural Science and/or Fisheries Economics and should also have extensive experience in the field of fisheries development Wide experience in commercial fisheries is also required Appointment for 2 years

SALARY, subject to U K income tax, in range of £3,500 to £4,000 plus a variable tax free overseas allowance in range of £795 to £1,550 per annum

Other benefits include free family passages, paid leave, children's education allowances and free accommodation and medical attention

For full details, application form and booklet about Sierra Leone, please apply giving age and brief details of qualifications and experience to

Appointments Officer,
Foreign and Commonwealth Office,

Overseas Development Administration
Room E301/N, Eland House, Stag Place,
London SW1E 5DH (419)

TANZANIA NATIONAL PARKS

SERENGETI RESEARCH INSTITUTE

Applications are invited from qualified candidates for the post of

DEPUTY DIRECTOR

with the Serengeti Research Institute Preference will be given to a candidate with a good advanced degree (preferably a Ph D) in the field of terrestrial ecology and considerable research experience in that field Experience and interest in the ecology of African game mammals will be an advantage

Duties will include

1. Assisting the Director in the day to day running and administration of the Institute
2. Acting as Director when the latter is away
3. Carrying out his own research project within the general framework of the Institute's research priorities as approved by its Scientific Council and the Board of Trustees of Tanzania National Parks

Salary according to qualifications and experience within the range of T Shs 34,000/=×1,500 to T Shs 38,500/= per annum

Applications in triplicate and typed which should include a full curriculum vitae and names of three referees qualified to give a realistic assessment of the candidate, and to reach the undersigned not later than September 30, 1973

The Chairman, Board of Trustees,
Tanzania National Parks
c/o Director, Serengeti Research Institute,
P O Seronera, Via Arusha, Tanzania, East Africa (384)

CSIRO

AUSTRALIA

DIVISION OF PROTEIN CHEMISTRY

APPOINTMENT OF CHIEF OF DIVISION

The Executive of the Commonwealth Scientific and Industrial Research Organization invites applications from scientists interested in the position of Chief, Division of Protein Chemistry The vacancy has been created by the appointment of Dr F G Lennox to the position of Chief Scientific Liaison Officer in London The Division, which is located in Parkville, close to the city of Melbourne, has a research staff of some sixty scientists, comprising mainly biochemists, with an equal number of ancillary staff

Within the framework of the Wool Research Laboratories, the Division is closely associated with the Division of Textile Industry in Geelong, Victoria, and the Division of Textile Physics in Sydney, New South Wales, in research to aid the Wool Industry Co-ordination of the work and co-operation with the International Wool Secretariat is the responsibility of the Chiefs of the three Divisions meeting in Committee The Chairman of the Committee is Dr M Lipson of the Division of Textile Industry

The programme of the Division includes research on the structure and chemistry of the keratins, the photodegradation of proteins including development of light-fast dyes and fluorescent compounds, and development of new and improved techniques for protein analysis

The Division also has programmes concerned with enzymes and muscle proteins, with collagen and the manufacture of leather, with seed proteins and with biologically-active proteins including antigens, hormones and virus proteins

The Chief of the Division is responsible for the conduct and direction of the research activities, for the general administration of the Division and for the control of funds available to it The Chief is expected to make recommendations to the Executive on the future orientation of the research programmes. The appointee should have an established record of personal research achievement and leadership in an appropriate field

Salary for the position will not be less than $A19,718 per annum

The tenure of the position is subject to negotiation The possibility of either a fixed term (of the order of seven years) or indefinite appointment could be discussed with the successful applicant In either event Superannuation privileges would be available

Further information on the Division's activities can be obtained by writing to the **Secretary (Administration), CSIRO, P.O. Box 225, DICKSON, A.C.T., Australia, 2602.**

Applications should contain a résumé of qualifications and research experience, the names of at least two referees, and should be directed to the above address by the *12th October, 1973*

(404)

GUY'S HOSPITAL
London, S E I

GROUP CHIEF PHYSICIST

£4740–£5445

To take charge of the Department of Clinical Physics and Bioengineering providing a broad range of physics services to the Guy's Group of Hospitals This is a Top Grade Post and an extensive experience in Medical Physics (preferably broadly based) at a level equivalent to that of Principal Physicict is required

Applications (with names of 2 referees please) to Personnel, Guy's Hospital, London, SE1 9RT

Guy's
HOSPITAL GROUP

THE QUEEN'S UNIVERSITY OF BELFAST

DEPARTMENT OF BOTANY

RESEARCH ASSISTANT

Applications are invited from graduates in Botany or Biochemistry to work with Professor Simon on problems of membrane structure and function in plants

Appointment will be on the salary scale £1,050-£1,629 for one year, from October 1, 1973, with the possibility of renewal for up to two further years

Further particulars may be obtained from Professor E W Simon, Department of Botany, The Queen's University of Belfast, Belfast 7 Applications, together with the names of two referees, should be sent to Professor Simon by September 3, 1973

(447)

UNIVERSITY OF THE SOUTH PACIFIC

FIJI

Applications are invited for post of (a) READER or (b) SENIOR LECTURER IN PHYSICS in the School of Natural Resources, tenable from the beginning of 1974 Applicants should have a sound bacbground in general Physics, a strong interest in teaching at university level and research interests and experience in the area such as Soil Science, Oceanography, Meteorology, Hydrology or Biophysics Duties of appointee will include (1) The development and teaching of courses in Physics which provide an understanding of the basic concepts of Physics within the context of a general education in science, an emphasis on the use of Physics in the application of science to the development of the use of natural resources of the region, a preparation for teachers of general science and physics in the secondary schools of the region (2) The development of research in one or more areas of environmental physics (3) Assisting the Head of the School in the overall administration and development of the School

Salary scales (a) $F8,300-$F8,800 per annum (b) $F6,700-$F7,900 per annum (£1 Sterling=$F1 99) 10% annual gratuity for contract appointment, superannuation contributions, partly furnished accommodation at rental of 15% of salary, appointment allowance Contracts may be for 2, 4 or 6 years

Details of form of application, further particulars and outline of terms of service are obtainable from The Registrar (Post 73/22), University of the South Pacific, P O Box 1168, Suva, Fiji Closing date September 20, 1973

(385)

UNIVERSITY OF MASSACHUSETTS

POLYMER ENGINEER

An important position in the School of Engineering at the University of Massachusetts, Amherst, has been made available Applications will be welcome from candidates who are sufficiently qualified for a teaching position at the assistant or associate professor level, and whose research interests lie in the areas of polymer fabrication or macroscopic solid state properties The successful candidate would be expected to work closely with the Polymer Science and Engineering Program and to initiate joint research projects Applicants must have relevant experience in polymers and preferably teaching experience in Engineering

Prospective applicants should submit their resumes to the Chairman of the Search Committee, Polymer Science and Engineering Program, University of Massachusetts, Amherst, Massachusetts 01002 We are an equal opportunity, affirmative action employer

(277)

AGRICULTURAL RESEARCH COUNCIL

POULTRY RESEARCH CENTRE

Applications are invited for a post in the Ethology Section within the Scientific/Higher Scientific Officer grades at the Poultry Research Centre, initially for work on the physiological changes accompanying frustration and conflict in fowls

Candidates should have a good Honours degree or preferably a Ph D, and be interested in establishing techniques for studying physiological parameters using radiotelemetry, the use of small computers for real-time analysis of multi-parametric systems and the presentation of these data to batch computer for further analysis

Salary within the scales £1,318-£2,177 or £2,076-£2,667 per annum with placement according to qualifications and experience F S S U Superannuation with a non-pensionable allowance to offset contributions

Application forms, which may be obtained from the Secretary, Poultry Research Centre, King's Buildings, West Mains Road, Edinburgh EH9 3JS, should be completed and returned to him not later than September 14, 1973

(450)

The University of Leeds
DEPARTMENT OF PHYSICS
SOLID STATE PHYSICIST

A vacancy exists for a POSTDOCTORAL RESEARCH FELLOW to work in a group using the de Haas-van Alphen Effect to study the effect of pressure on alkali metals Previous experience in solid state physics is necessary and a knowledge of low temperature techniques desirable

The research will be supported by the SRC for a period of three years from September 1973 Salary range £1,764-£2,079 (with FSSU)

Applications, containing a curriculum vitae and the names of two referees, should be sent as soon as possible to Mrs M Westwood, Administrative Assistant, Department of Physics, University of Leeds, Leeds LS2 9JT (372)

ROTHAMSTED EXPERIMENTAL STATION
HARPENDEN, HERTS AL5 2JQ

The Soil Survey of England and Wales (Harrogate Centre) requires a RESEARCH SCIENTIST to map soils A good degree in chemistry, geography, soil science or environmental science is required

Appointment in grade of Scientific Officer (£1,590 to £2,177) or Higher Scientific Officer (£2,076 to £2,667) Starting salary in accordance with qualification and experience At least two years' post-qualification experience required for appointment in the higher grade F S S U with allowance to off-set contributions

Applications, naming two referees and quoting reference 1972 to the Secretary by September 28, 1973 (430)

U M I S T
DEPARTMENT OF BIOCHEMISTRY
SPECIAL RESEARCH ASSISTANT

Applications are invited, preferably from candidates with a Ph D degree and research experience in the purification of enzymes, to work on a S R C project concerned with the constitution and synthesis of pyruvate carboxylase in thermophilic bacteria The appointment will be for a year in the first instance with the possibility of renewal for a further 2 years

Starting salary £1,929 to £2 058 per annum with F S S U

Apply with two referees, quoting reference number B10/381/G to Dr T K Sundaram, Department of Biochemistry, University of Manchester Institute of Science and Technology, Sackville Street, Manchester M60 1QD, as soon as possible (428)

QUEEN ELIZABETH COLLEGE
(UNIVERSITY OF LONDON)
Campden Hill Road, W8 7AH

GRADUATE RESEARCH ASSISTANT required in the Chemistry Department to help academic staff with the administration of a spectroscopy laboratory and a learning aids laboratory, and to give some tuition to graduate students Salary range £1,572 to £1,749

Apply to Professor L Hough. (407)

UNIVERSITY OF BIRMINGHAM
INSTITUTE OF CHILD HEALTH

BACTERIOLOGY TECHNICIAN required to assist in studies of malabsorption syndromes in young children Experience of anaerobic culture techniques essential

Salary up to £2,028 per annum

Reference 854/B/835

Apply Assistant Secretary (Personnel), University of Birmingham, P O Box 363, Birmingham B15 2TT (390)

UNIVERSITY OF EDINBURGH
DEPARTMENT OF BOTANY

Applications are invited for an S R C sponsored POSTDOCTORAL RESEARCH FELLOWSHIP, available from October 1, 1973, to collaborate on a study of the synthesis and function of polydisperse R N A in higher plants Experience with R N A polymerase, hybridization and general nucleic acid technology is desirable The starting salary will be within the range £1,764-£2,079 per annum, and may be renewed for a second year

Applications with *curriculum vitae* and the names of two referees should be sent, as soon as possible, to Dr J Ingle, Department of Botany, The King's Buildings, University of Edinburgh, Mayfield Road, Edinburgh EH9 3JH Please quote reference 5064 (448)

UNIVERSITI SAINS MALAYSIA
PENANG, MALAYSIA

Academic Appointments

Applications are invited for the following posts

A. SCHOOL OF PHARMACEUTICAL SCIENCES
Professor in the fields of
Pharmacy, Pharmaceutics, Pharmaceutical Chemistry, Pharmacology, Physiology and Pharmaceutical Technology
Senior Lecturers/Lecturers in the fields of
Pharmaceutical Technology, Pharmacology and Pharmaceutical Chemistry

B. SCHOOL OF PHYSICS AND MATHEMATICS
Professors in the fields of
Applied Mathematics and Pure Mathematics
Senior Lecturers in the fields of
Solid State Physics, Biophysics and Pure Mathematics
Lecturers in the fields of
Geophysics, Biophysics, Electronics, Solid State Physics, Computer Science, Statistics/Biometrics, Pure Mathematics and Applied Mathematics

C. SCHOOL OF APPLIED SCIENCES
Lecturers in the fields of
Silicate-based Technologies and Metallurgy

D. SCHOOL OF BIOLOGICAL SCIENCES
Senior Lecturers in the fields of
Entomology (in the fields of Applied Entomology related to agricultural, forestry, medical or veterinary aspects geared towards the prevention and control of the arthropod vectors and pests)
Parasitology (in the fields of Applied Parasitology involving parasites of medical, veterinary, agricultural, fisheries or related fields, their economic importance, methods of prevention and control of parasitic diseases in the context of national developmental programmes)

E. SCHOOL OF CHEMICAL SCIENCES
Professor in the field of Inorganic/Physical Chemistry
Senior Lecturers in the fields of
Inorganic/Analytical Chemistry and Organic Chemistry
Lecturers in the fields of
Inorganic Chemistry, Organic Chemistry and Physical Chemistry

F. SCHOOL OF HOUSING, BUILDING AND PLANNING
Senior Lecturers/Lecturers in the fields of
Building Construction, Materials and Systems, Structural Engineering, Basic design and Graphics, Statistics, Operational Research and Computers, Environmental physics, Housing and community design and planning, Urban and Regional Planning with specialization in Socio-Economic Analysis and Development, Transportation and Public Utility Systems and Regional Development Planning

QUALIFICATIONS/EMOLUMENTS:
Professors

Should have a Ph D for the above-mentioned fields together with relevant teaching experience in institutions of higher learning and also the ability to set up an administration of the facilities pertaining to undergraduates and professional training

A Professor when appointed should command a salary within the range of M$27,120 (£4,773) to M$36 000 (£6,336) per annum The point of entry into the salary scale depends on qualifications, experience and family circumstances

Senior Lecturers:

For the appointment of Senior Lecturers, applicants must have a doctorate from a well established university, with several years of experience in research and teaching at university level together with publications of recognized academic standing

A Senior Lecturer when appointed should command a salary within the range of M$22,380 (£3,939) to M$30,120 (£5,301) per annum The point of entry into the salary scale depends on qualifications, experience and family circumstances

Lecturers.

A Lecturer normally should possess a Ph D in the relevant fields and when appointed a Lecturer should expect to command a salary within the range of M$16,800 (£2,957) to M$26,580 (£4,678) per annum The point of entry depends on qualifications, experience and family circumstances

OTHER BENEFITS:
Provident Fund and free medical

INITIAL APPOINTMENT:
Successful applicants may be given a three-year initial appointment, thereafter, subject to satisfactory service, their appoinment may be extended for another three years

Further information including advice regarding the method of application and on further particulars about terms and conditions of service should be obtained from The Registrar, Universiti Sains Malaysia, Minden, Penang, Malaysia

The closing date of receipt of applications is September 21, 1973 The University reserves the right to make appointment by invitation

REGISTRAR

(454)

MEDICAL RESEARCH COUNCIL
Clinical and Population Cytogenetics Unit

SCIENTIST

A vacancy for a research scientist will shortly become available in the Cytogenetics Section of the above Unit Applications are invited from graduates with a Ph D, or equivalent, in genetics or cytogenetics and an interest in the effects of environmental mutagens on human and other mammalian chromosomes Salary, dependent upon age, qualifications and experience, will be within the scale £1,688 to £3,192 with FSSU benefits

Applications in writing, giving full personal particulars and names of two referees, to the Administrative Office, MRC Clinical and Population Cytogenetics Unit, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, by September 14, 1973 (374)

Government of Malawi

Ministry of Agriculture and Natural Resources

requires

Hydrologist

Salary up to £3,474+tax free gratuity

Maximum emoluments equivalent to U K salary of £4,900

Required for the KARONGA RURAL DEVELOPMENT PROJECT to be responsible to the Project Manager for the establishment of a hydro-meteorological network over an area of approximately 400 square miles

Candidates, aged up to 50, should hold a degree in Civil Engineering or similar subject and post-graduate qualification in Hydrology He should have at least three years post-qualification experience preferably in irrigation and drainage

Paid leave with free passages and baggage allowance Education allowance and subsidised housing Loan for the purchase of a car Free medical attention

Apply to MALAWI BUYING AND TRADE AGENTS, Recruitment Section, Abbey House, 6 Victoria Street, London, SW1H OLA for application form and further particulars, quoting reference number 650/B. (397)

SCIENCE RESEARCH COUNCIL

The **RADIO AND SPACE RESEARCH STATION** has a vacancy for a **Research Associate**, tenable for a period of up to 3 years, in the Solar Physics Group of its Astrophysics Research Division, located at Culham Laboratory, Nr Abingdon

The work will involve the design and preparation of ultraviolet spectroscopic rocket experiments and participation in the relevant astrophysical problems including analysis of results

The successful candidate should have a good honours degree and preferably a Ph D Research experience in space research, astrophysics, spectroscopy, optics, or atomic physics, would be an advantage

Salary according to age, qualifications and experience but normally between £1,800 and £3,250

Apply for an application form to **The Secretary, Science Research Council, Radio and Space Research Station, Ditton Park, Slough SL3 9JX, Bucks**

Closing date September 30, 1973 (418)

CONGRESS

3rd International Congress of Plant Tissue and Cell Culture

21st–26th JULY 1974

UNIVERSITY OF LEICESTER, LEICESTER, ENGLAND

Plenary papers and shorter Concurrent papers covering

Physiology & Biochemistry	Tumours, Parasites & Symbionts
Growth & Cytodifferentiation	Genetics
Morphogenesis	Methodology

Research Demonstrations

Trade Exhibition

To obtain forms on which to offer papers or demonstrations and to book accommodation, the Programme and Abstracts, write to The Secretariat, IAPTC Congress, Botanical Laboratories, University of Leicester, Leicester, LE1 7RH (telephone 0533 50000), enclosing Registration Fee of £3 00 (cheques payable to IAPTC Congress Fund)

Participants intending to offer a paper or demonstration must first register and then return the appropriate forms **before 1st November, 1973.**

(409)

UNIVERSITY OF MANCHESTER INSTITUTE OF SCIENCE AND TECHNOLOGY

TECHNICIAN (GRADE 5)

(REF CH/375/AD)

Required in the Department of Chemistry to join a team engaged on interesting work in organic chemistry A knowledge of chemical theory to HNC level is desirable, but the requirements of the post place greater emphasis on practical ability in preparative chemistry The post will give the successful candidate the opportunity to learn special techniques used in the work, and to further his theoretical background

Salary within the scale £1,881 to £2,241 per annum

Requests for application forms, quoting Reference number, should be addressed to the Registrar, U M I S T, Sackville Street, Manchester M60 1QD, to be returned no later than September 7, 1973

(414)

UNIVERSITY OF GLASGOW

LECTURESHIP IN MICROBIOLOGY

Applications are invited for a Lectureship in Microbiology in the Faculty of Science The salary placement will initially be at the lower end of the Lecturers' scale of £1,929 to £4,548 per annum F S S U

Preference will be given to applicants with experience in microbial biochemistry and with research interests in that area or in microbial genetics or microbial pathogenicity

Applications (eight copies) should be lodged not later than October 15, 1973, with the undersigned from whom further particulars may be obtained

In reply please quote Ref No 3334 M

ROBT T HUTCHESON,
Secretary of the University Court

(362)

UNIVERSITY OF KEELE

JUNIOR RESEARCH FELLOW IN THE W E DUNN UNIT OF CARDIOLOGY

Graduate scientist with knowledge of ultrasonic and/or electronics required to join a small research team investigating the causes of brain damage during open-heart surgery The appointment will be initially for 3 years Ph D registration will be available Salary £1,398-£1,839 per annum according to experience

Application forms from the Registrar, The University, Keele, Staffs ST5 5BG, to whom they should be returned by October 1, 1973 (440)

UNIVERSITY OF IFE/ UNIVERSITY OF READING

JOINT FISHERIES RESEARCH PROJECT, LAKE KAINJI, NIGERIA

POSTDOCTORAL FELLOW required as Team Leader to supervise the research programme of five postgraduates at Lake Kainji and work on an aspect of fisheries biology Salary in scale £1 929-£3,048 per annum, plus an allowance whilst overseas TWO RESEARCH STUDENTSHIPS, to a value of £770 per annum, also available to investigate the lake invertebrates and their contribution of fish production The successful candidates will register at Reading for a higher degree The appointments are for three years from October 1, 1973 About two years will be spent at Kainji and the remainder at Reading

Apply, quoting Ref MN57, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH (445)

ASSISTANT EXPERIMENTAL OFFICER required for Chemistry Department, University of Reading, as soon as possible, to work on the development of advanced teaching experiments in Physical Chemistry, the training of junior technical staff and research in gas kinetics Hons degree in Chemistry of GRIC desirable Suitably qualified applicants may be permitted to work for a higher degree Salary in the scale £753-£2,043 per annum (under review)—Apply, quoting Ref TN 35 with names of two referees and details of qualifications and experience, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH (413)

TECHNICIAN

(well-qualified) required to work on a research project on the structure of immunoglobulins Salary (currently* under review) from £1,416 per annum including London Weighting Applications to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, quoting Ref C H 3 (446)

GOVERNMENT OF HONG KONG

Research Officer (Fisheries)

Required for one tour of 2½ years initially Annual salary will be in scale rising to approximately £5750 according to qualifications and experience Substantial gratuity Free passages Liberal leave on full salary Generous education allowances and holiday visit passages Government quarters at moderate rental

Candidates, preferably under 35 years of age, MUST have a First or Second Class Honours Degree in Chemistry or Physics from a Hong Kong or British University, and at least one year's post-graduate experience in fisheries research work The officer will form part of a research team investigating fisheries problems including hydrological, oceanographic and other studies

For further particulars you should apply, giving brief details of experience to

crown agents

M Division, 4 Millbank, London SW1P 3JD, quoting reference number M/3F/7306205/NF. (399)

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UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF CHEMISTRY

BIOCHEMIST-ENZYMOLOGIST

Applications are invited from biochemists (preferably at the Ph D level) for the post of enzymologist working in collaboration with Professor A R Battersby Dr J Staunton and Dr E McDonald, on a range of enzyme systems particularly dehydrogenases, hydroxylating systems, amine oxidases and the enzymes involved in the biosynthesis of haem, vitamin B_{12} and related pigments

The post is an Assistantship in Research of the University of Cambridge and appointment will be from October 1, 1973, or from a date to be agreed, for up to five years within the scale £1,752 by four annual increments to £2 388, together with FSSU benefits the point selected on the scale depends on age and experience Applications naming two referees, should be sent as soon as possible but not later than September 19 1973 to Professor A R Battersby, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW (telephone 0223-66499) from whom further information can be obtained (369)

FOOD R A

SENIOR MICROBIOLOGY TECHNICIAN

Senior Technician with H N C (Applied Biology), A I M L T, A I A L T or similar qualification required for work in the Botulinum Laboratory Experience in small animal work and in bacteriological techniques desirable Salary according to age and qualifications Excellent fringe benefits

Apply in writing to

The Deputy Director,
Food RA
Randalls Road,
Leatherhead
Surrey KT22 7RY,

quoting ref EHS/15 (431)

UNIVERSITY OF QUEENSLAND

AUSTRALIA

READER/SENIOR LECTURER IN MATHEMATICS (STOCHASTIC PROCESSES)

Qualifications An applicant should have a distinguished academic record, have published significant contributions in the field of Stochastic Processes and should also have considerable teaching experience

Salary Reader—$A15,940 per annum Senior Lecturer—$A12,268-$A14,308 per annum

Other Benefits Superannuation similar to F S S U, housing assistance, study leave, and travelling and removal expenses

Additional information and application forms are obtainable from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square London WC1H 0PF

Applications close in London and in Brisbane on September 28, 1973 (436)

WEST OF SCOTLAND AGRICULTURAL COLLEGE

SENIOR LECTURER/LECTURER IN HORTICULTURE

Applications are invited from graduates in Horticulture Horticultural Science or related disciplines for a post of Senior Lecturer or Lecturer in Horticulture, mainly in connexion with the Honours B Sc degree in Horticulture offered by the University of Strathclyde in conjunction with the College

For officers of sound experience and over thirty-one years of age salary will be on the Grade II Scale —£3 377-£4,057 For others (according to age, qualifications and experience) on either Grade III—£2 087-£3,640 or Grade IV—£1,402 (Honours Graduates £1 499) rising to £1,925

Conditions of appointment and application forms are available from the Secretary, Auchincruive, Ayr, KA6 5HW, with whom applications should be lodged not later than September 10, 1973 (406)

PRE AND POST DOCTORAL POSITIONS available for studies on changes in protein synthesizing system, with special emphasis on Ribosomes—topography, biogenesis and function—under various conditions of growth and development Teaching opportunities available Send resume to B H Sells, Director of Laboratories of Molecular Biology, Faculty of Medicine Memorial University, St John's, Newfoundland Canada (389)

UNIVERSITY NOT FOR YOU?

If you have "O" or "A" level science and don't want to go to college why not train as a technician We have immediate vacancies to H N C level Ring or write Liz Robinson, Walbrook Appointments, 116 High Holborn, W C 1 01 405 8787 (452)

UNIVERSITY OF ABERDEEN

RESEARCH ASSISTANT required from October 1, 1973, for the Unit for Research on Addictive Drugs Minimum qualifications Second Class Honours Degree in Pharmacology, Physiology or Pharmacy Salary on scale £1,305×87—£1,479×90—£1,659 with placing according to qualifications Appointment for one year in first instance, renewable for two further years Enrolment for a Higher Degree will be encouraged

The research project deals with the assessment of the potencies of new narcotic analgesic drugs, their structure-activity relationships and the development of new assay methods

Further particulars from The Secretary, The University, Aberdeen, with whom applications (2 copies) with curriculum vitae and names of two referees should be lodged by Sptember 14, 1973 (394)

QUEEN ELIZABETH COLLEGE

(UNIVERSITY OF LONDON)
Campden Hill Road, W8 7AH

RESEARCH DEMONSTRATOR IN PHYSIOLOGY

Applications are invited from graduates, preferably in physiology, for a student demonstratorship (£695 plus fees and payment for demonstrating) Preference will be given to applicants interested in the effect of snake venom upon the mechanisms of coagulation and fibrinolysis

Applications should be sent to Professor J A C Knox Physiology Department, by September 5 (386)

NATIONAL VEGETABLE RESEARCH STATION

SENIOR STATISTICIAN

There is a vacancy for a Senior Statistician (Biometrician) to advise on statistical and mathematical methods, including the writing of computer programs Opportunities for research

A good Honours degree and at least three years' relevant post-graduate experience are required Appointment in grade of Higher Scientific Officer (£2,076-£2,667) to Senior Scientific Officer (£2,615-£3,640), according to experience FSSU with 4½% allowance to offset contributions

Full particulars and application form (to be returned by September 14 1973) from the Secretary, NVRS, Wellesbourne, Warwick (377)

UNIVERSITY COLLEGE LONDON

DEPARTMENT OF BOTANY AND MICROBIOLOGY

Applications are invited for the post of RESEARCH ASSISTANT, GRADE II, to stay initially for one year and renewable for a total of up to three years at a salary of £1,929 plus £162 London Allowance The person should be a post-doctoral biochemist or a molecular biologist experienced in nucleic acids and/or DNA polymerases and repair enzymes

Applications to Assistant Secretary (Personnel) (N), University College London, Gower Street, London WC1E 6BT, from whom further particulars may be obtained (425)

JUNIOR TECHNICIAN required to assist in biochemical research laboratory Knowledge of auto-analyser and gel chromatography techniques an advantage—Application, together with names and addresses of two referees, to Professor H E de Wardener, Department of Medicine, Charing Cross Hospital Medical School, Fulham Palace Road, London W6 8RF (381)

GRADUATE RESEARCH ASSISTANT and JUNIOR TECHNICIAN required in THE TISSUE CULTURE AND CYTOGENETICS UNIT Relevant experience desirable but not essential as adequate training will be given Applications with the names of two referees should be made to Dr D C Williams, Research Department, Marie Curie Foundation, The Chart, Oxted, Surrey, by September 7 (427)

UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF ZOOLOGY

A RESEARCH ASSISTANT is required for the Museum of Zoology The person appointed will be responsible to the Director of the Museum and the main duty will be to set up a permanent exhibition of various aspects of entomology and insects that are the subject of current teaching and research in the Faculty Preference will be given to candidates of immediate post-doctoral standing and the person appointed will have the opportunity to pursue his own research Salary will be within the range £1,320 to £3,192

Further details may be obtained from the Secretary, Department of Zoology, Downing Street, Cambridge CB2 3EJ Closing date for all applications, September 1973 (423)

UNIVERSITY OF CAMBRIDGE

A post is available in the Department of Experimental Psychology for a RESEARCH ASSISTANT to work on problems of visual perception The appointment, which is associated with an M R C grant, is for three years from October, 1973 The salary will be appropriate to experience and qualifications, but may be up to £1,923 (by £156 to £2,079, by £159 to £2,238) per annum

Preference may be given to candidates, postgraduate or postdoctoral, who have been trained in Engineering or in Physics and who wish to work in the biological sciences Some experience of optics or of electronics or of computing would be especially valued Applicants should write to Dr J Mollon, Department of Experimental Psychology, Downing Street, Cambridge CB2 3EB, and should enclose a curriculum vitae and the names of two referees (453)

FELLOWSHIPS AND STUDENTSHIPS

Liverpool School of Tropical Medicine

(UNIVERSITY OF LIVERPOOL)

RESEARCH STUDENTSHIPS

Research studentships are available in the Department of Parasitology in connection with the following projects

1 Drug resistance and chemotherapy in malaria, with particular reference to the mode of action of antimalarial drugs
2 Chemotherapy of leishmaniasis
3 Nucleic acids of parasitic protozoa

The studentships are available from October 1, 1973 Applicants should possess a good Honours degree in the Natural Sciences The successful appointees will be expected to register for a higher degree The value of the studentship is equivalent to S R C rates

Applications giving full details of qualifications and the names of two academic referees, should be sent without delay to the Head of the Department of Parasitology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA (451)

UNIVERSITY OF GLASGOW

CEGB POST-DOCTORAL RESEARCH FELLOWSHIP

Applications are invited for this post in the Kelvin Laboratory, East Kilbride The Fellowship is provided by the Central Electricity Generating Board to stimulate research with the 130 Mev Electron Linear Accelerator on topics not otherwise included in the experimental programme Previous work has involved measurements of neutron cross sections with nanosecond time-of-flight techniques Extension to microsecond timing could lead to solid state studies Other suggestions will be considered Extensive programmes in electron scattering, photonuclear and electrofission studies are already in progress

Salary according to qualifications and experience on the Lecturer scale £1,929 to £4,548 per annum, with FSSU membership

Further particulars can be obtained from Professor G R Bishop, Department of Natural Philosophy, University of Glasgow, Glasgow G12 8QQ

Closing date for applications September 15, 1973 (420)

UNIVERSITY OF NEWCASTLE UPON TYNE

DEPARTMENT OF ORGANIC CHEMISTRY

Applications are invited from graduates with a good Honours degree in Chemistry for a Research Studentship to work on the organic chemistry of penicillins The award which will be equivalent in value to that of an SRC Research Studentship, will be available from October 1, 1973, and the successful candidate will be expected to register for the Ph D degree

Further details may be obtained from Dr R J Stoodley, Department of Organic Chemistry, The University, Newcastle upon Tyne NE1 7RU, to whom applications, together with names and addresses of two referees, should be sent as soon as possible (367)

University of Leeds

ASTBURY DEPARTMENT OF BIOPHYSICS

Applications are invited for a POST-DOCTORAL RESEARCH FELLOWSHIP funded by the S R C The work will be carried out under the direction of Dr J E Lydon, and will involve the development of an X-ray diffraction camera for the study of liquid crystal phases and its subsequent use in investigating temperature transitions and transient states Applicants should hold a Ph D degree and preferably have experience in physical methods of studying structure The appointment will be made for one year in the first instance from October 1, 1973, with possible renewal for a further two years Starting salary £1,764 (under review)

Applications, including the names of three referees, should be made by September 10, 1973, to Professor A C T North, Astbury Department of Biophysics, University of Leeds, Leeds LS12 9JT (429)

NEW ZEALAND

UNIVERSITY OF CANTERBURY

CHRISTCHURCH

UNIVERSITY POST-DOCTORAL FELLOWSHIP

BOTANY

Applications are invited for a University Post-doctoral Fellowship in the above-mentioned department

Applicants should possess a Ph D or equivalent degree, preferably followed by some research experience An appointee may be asked to undertake a limited amount of teaching in addition to contributing to the current research programme in his particular field

The emolument will be $NZ5,500 per annum Fellowships are tenable normally for one year, but with the possibility of extension

Further particulars and Conditions of Appointment may be obtained from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

Applications close on September 30, 1973 (434)

UNIVERSITY OF EAST ANGLIA

SCHOOL OF CHEMICAL SCIENCES

Applications are invited for a post-doctoral fellowship to work in collaboration with Dr A J Thomson to investigate the mechanism of action of anti-tumour platinum compounds The fellowship is tenable for two years from October 1, 1973, or as soon after this date as possible, at a salary on the scale £1,929-£2,058 plus FSSU

Applications, as soon as possible, giving the names of two referees, to the Senior Administrative Assistant, School of Chemical Sciences, University of East Anglia, Norwich NOR 88C (400)

UNIVERSITY OF SHEFFIELD

DEPARTMENT OF CHEMISTRY

Applications are invited from first or upper second class honours graduates in Chemistry or Biochemistry for an Agricultural Research Council Studentship The appointment will be for 3 years commencing October 1, 1973, and the successful candidate will study aspects of the biosynthesis and metabolism of plant proanthocyanidins It is expected that the student will register for a higher degree for which fees are paid

Applications, together with the name of one referee, should be sent as soon as possible to Dr E Haslam, Reader in Organic Chemistry, Department of Chemistry, University of Sheffield, Sheffield S3 7HF Quote Ref R67/G (388)

UNIVERSITY OF BRISTOL

SCHOOL OF CHEMISTRY

Postdoctoral Research Fellowship in Organic Mass Spectrometry Appointment for one year on a salary of £1,929 per annum or £2,058 per annum (scale effective from October 1, 1973) This work will involve the further development of a computerized (PDP8) gas chromatography-mass spectrometry (GC-MS) system and its application to the analysis of complex lipid extracts from oragnisms and sediments Experience in m s is essential and a knowledge of GC-MS and mini computers is desirable

Applications, including the names of two referees, to Professor Geoffrey Eglinton, Organic Geochemistry Unit, School of Chemistry, Bristol BS8 1TS (410)

Wellcome

Studentship

Wellcome Foundation and York University

Applications are invited from graduates holding first or upper second class degrees in Biochemistry or Chemistry to do research which would lead to an award for a Ph.D on the mechanism of the binding of insulin to its receptor

The work will be carried out jointly in the Wellcome Foundation's Diabetes Research Laboratory at Dartford (Dr Lazarus) and in the Chemistry Department of York University (Drs Garratt and Penzer)

Further details and application forms may be obtained from

Site Personnel Officer (RPW),
THE WELLCOME FOUNDATION LTD.,
Temple Hill,
Dartford,
Kent
Tel Dartford 23488, ext 260

(442)

ULSTER • THE NEW UNIVERSITY

SCHOOL OF PHYSICAL SCIENCES
(CHEMISTRY)

RESEARCH FELLOWSHIP

Applications are invited for an SRC-sponsored Research Fellowship in the field of Physical-Organic Chemistry The work will involve kinetic investigation of electrostatic effects in Organic reaction mechanisms (in association with Dr A C Knipe)

The appointment will be for a 1 year period at a salary of £1,764 per annum (with FSSU)

Further particulars may be obtained from The Registrar, The New University of Ulster, Coleraine, Northern Ireland (quoting Ref 73/90) to whom applications, including the names and addresses of three referees, should be sent as soon as possible (370)

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF MATHEMATICS

SEMICONDUCTOR THEORY

Applications are invited for RESEARCH STUDENTSHIPS supported by the Science Research Council, which are available for theoretical work to investigate recombination and related problems by use of quantum mechanics and statistical mechanics There will be contact with experimental work at Ferranti Limited and with government research laboratories Posts are tenable for up to three years, commencing as soon as possible

A good honours degree in Mathematics, Physics, Engineering Science or similar qualifications is essential and registration for an M Phil or a Ph D degree is encouraged

Please apply as soon as possible, giving the name of a referee to

Professor P T Landsberg,
Department of Mathematics,
University of Southampton,
Southampton,
SO9 5NH (441)

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF PHYSICS

Applications are invited for a post-doctoral research Fellowship to engage upon a study of the surface properties of fingerprints The work involves the use of a Stereoscan microscope The appointment will be for a period of one year Salary from £1,764 per annum (under review), depending on experience, with FSSU benefits

Applications, together with a brief curriculum vitae and the names of two referees, should be sent to the Deputy Secretary, The University, Southampton SO9 5NH, as soon as possible Please quote reference number Na 266/73/R (366)

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of RESEARCH STUDENT to work on the development of techniques of scanning electron microscopy of oral mucous membrane, in the School of Dental Surgery There will also be some opportunity to become acquainted with the techniques of transmission electron microscopy

The appointment will be for one year in the first instance but it is hoped that progress will allow of the renewal of the appointment for a further period The student, who will be expected to register for a higher degree, will probably be a recently qualified graduate in one of the biological sciences

Salary comparable to those of the Research Councils (currently £675 per annum nett) and it is hoped that the appointment will be taken up in the Autumn term 1973

Applications, stating age, qualifications and experience together with the names of two referees, should be received as soon as possible by The Registrar, The University, P O Box 147, Liverpool L69 3BX Quote Ref RV/80425/N (373)

UNIVERSITY OF SUSSEX
SCHOOL OF BIOLOGICAL SCIENCES

RESEARCH FELLOWSHIP IN INVERTEBRATE NEUROPHYSIOLOGY

Applications are invited from post-doctoral neurophysiologists to take part in an MRC supported project concerned with the growth and development of the molluscan nervous system

Preference will be given to Ph D s with experience in intracellular recording techniques which may have been obtained on vertebrate or invertebrate animals

The post is available from October 1, 1973, and will last for three years The salary will be in the range £1,764-£2,079 per annum

Further particulars and application forms can be obtained from the Secretary of Science, Science Office (E), University of Sussex, Falmer, Brighton BN1 9RH (379)

THE OPEN UNIVERSITY
Faculty of Science

RESEARCH STUDENTSHIP IN PHYSICS

Applications are invited for a Research Studentship tenable from 1st September or as soon as possible thereafter in one of the following research areas

1 Energy Research The application of thermodynamic principles to the production and utilization of energy on an industrial scale with a view to identifying ways of conserving energy

2 Biophysics X-ray diffraction and micro electrode measurements on muscle and cornea

3 Building Science The physical techniques of the scale modelling of buildings with a view to optimizing thermal, acoustic and lighting properties

Applicants should possess an honours degree (first or second class) in Physics The value of the studentship is £695 (plus the usual allowances)

Further particulars and application forms etc , are available from the **Higher Degrees Office, The Open University, P O. Box 49, Walton Hall, Milton Keynes, MK7 6AD.** Closing date Friday, 7th September, 1973

(432)

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF CHEMISTRY

The Photochemistry of Biologically and Industrially Important Molecules

Applications are invited from individuals holding an honours degree in Chemistry or GRIC to carry out postgraduate work on the photo-degradation of wool The value of this studentship will be £695 per annum , the student will be required to enter candidature for Ph D

Applications, giving curriculum vitae with the names of two referees, should be addressed to Dr K Salisbury, Department of Chemistry, The University, Southampton SO9 5NH (364)

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF PHYSICS

Applications are invited for a post-doctoral research Fellowships to study electron excitation in solids by slow-electron energy-loss spectroscopy Experience in surface physics or slow electron atom scattering would be an advantage The appointment will be for a period of two years The salary will be £1,764 in the first year and £1,923 in the second (under review) with FSSU benefits

Applications, giving a brief curriculum vitae and the names of two referees, should be sent to the Deputy Secretary's Section (Ext 2400), The University, Southampton S09 5NH, as soon as possible Please quote reference number Na 268/73/R (365)

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P J LeBlanc and A L Jackson

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E J Perkins, E Gribbon and J W M Logan

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J S Young and C. I Gibson

Edited by Professor R B Clark, Department of Zoology, The University, Newcastle upon Tyne, NE1 7RU, England

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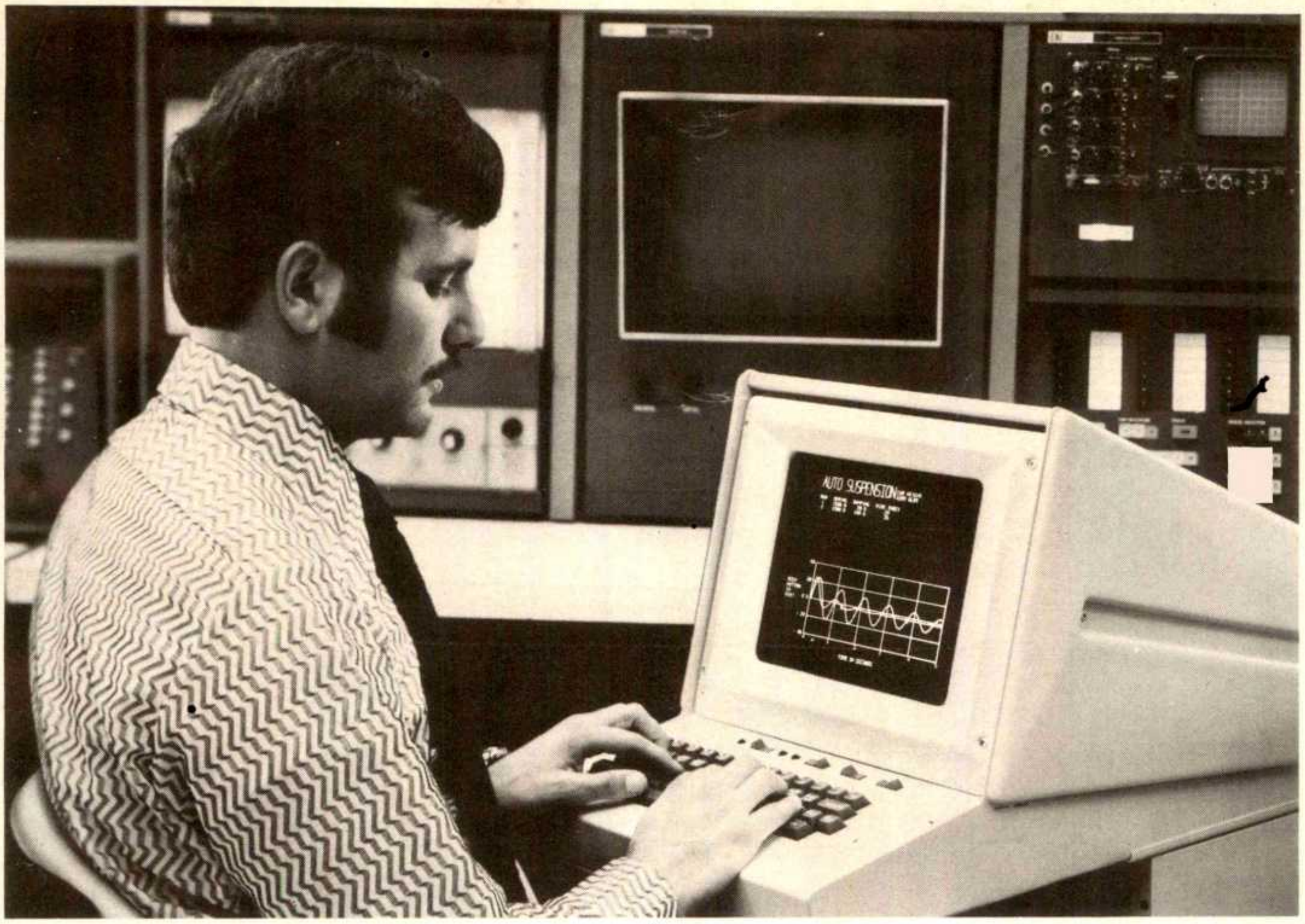

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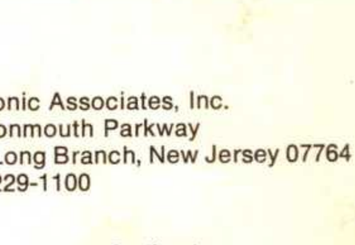

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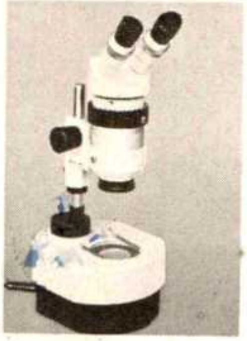

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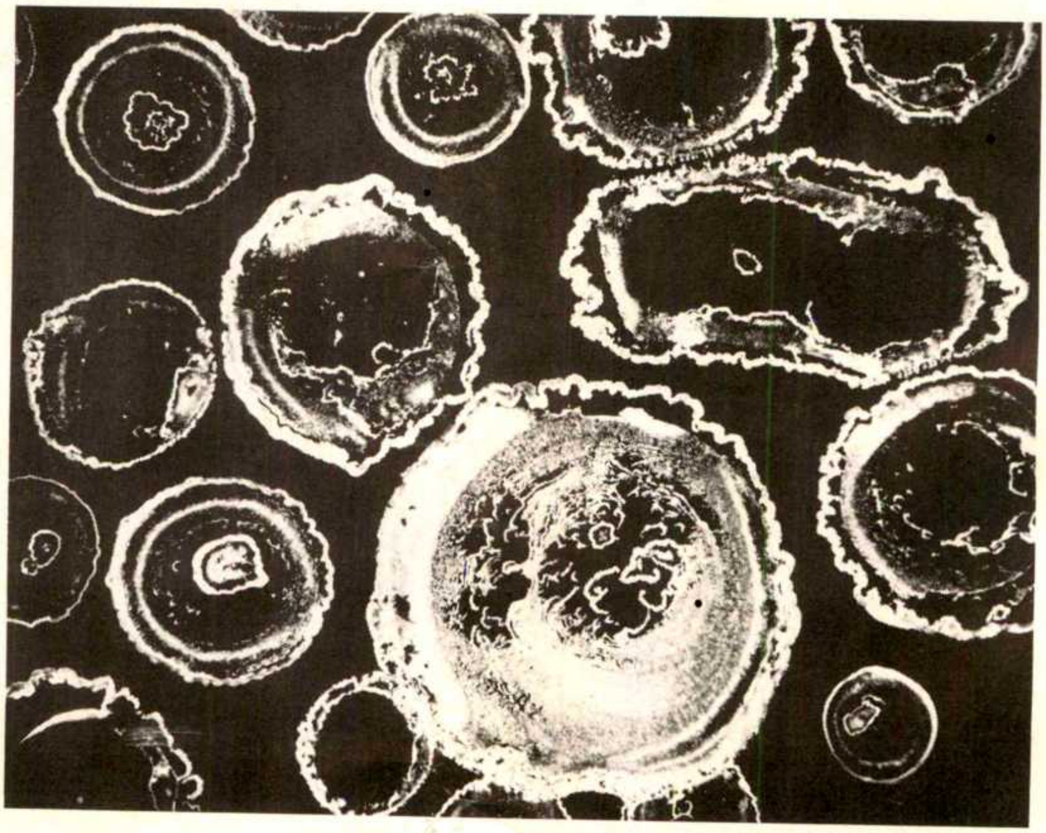

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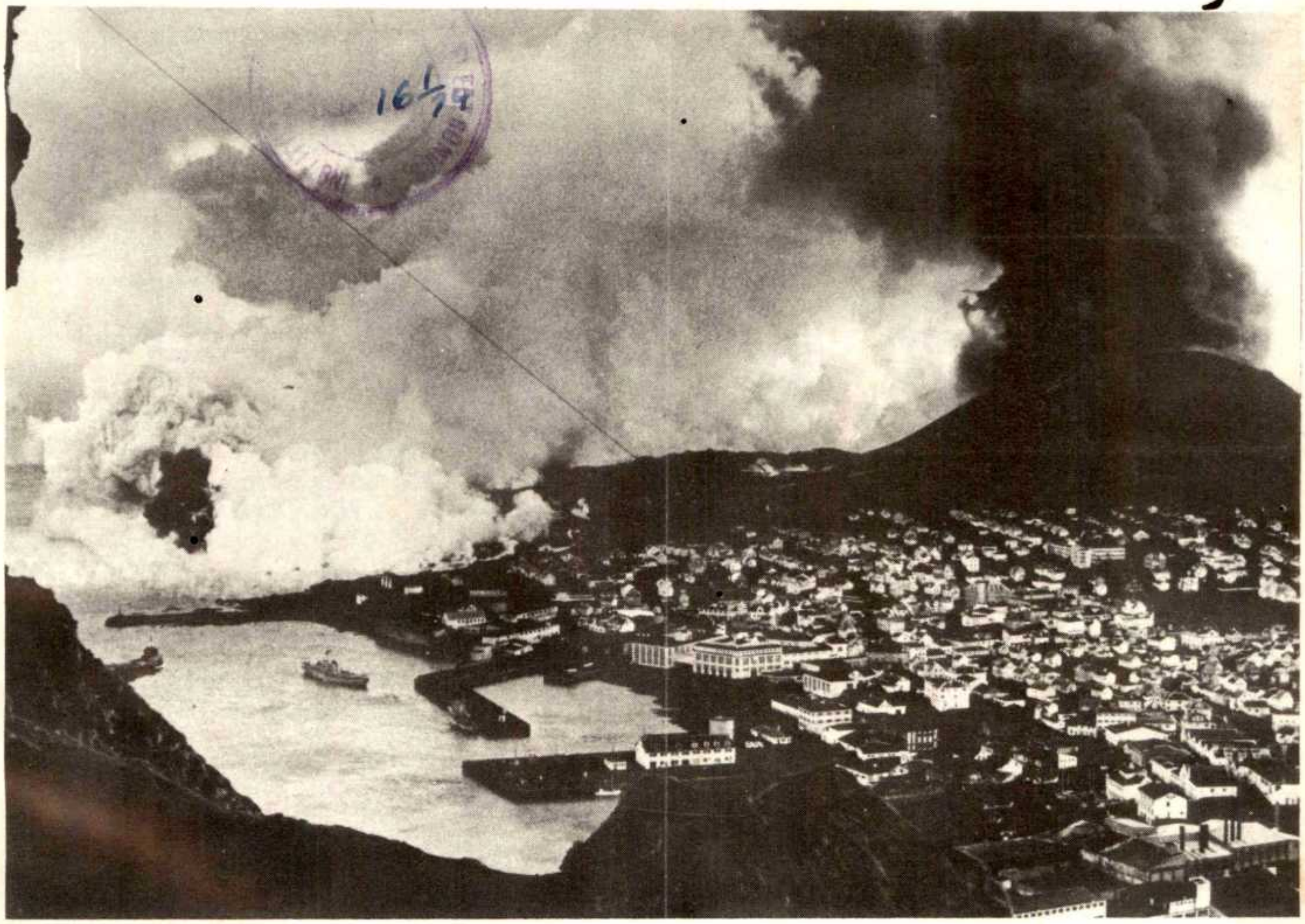

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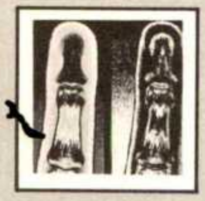

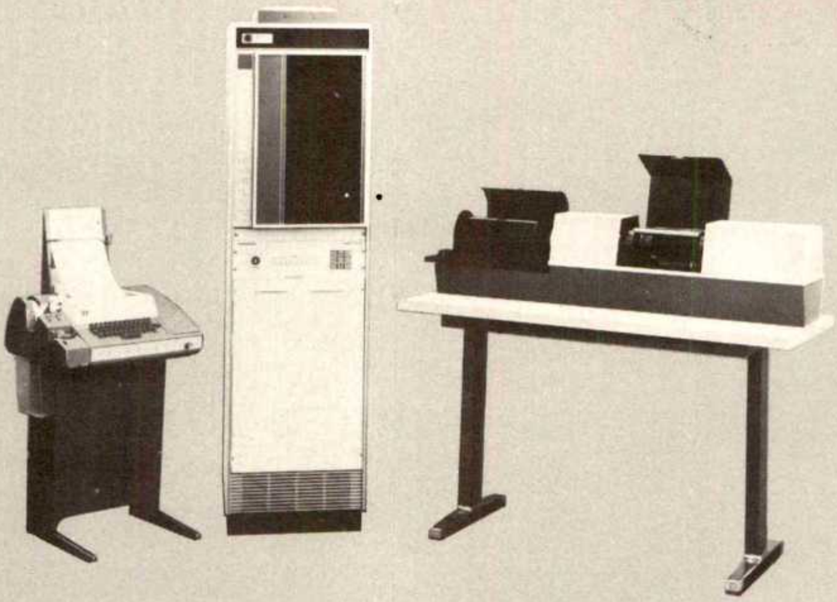

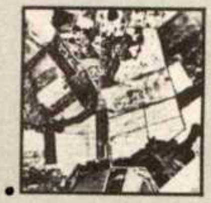

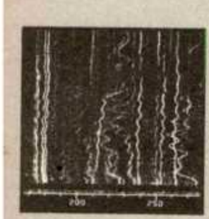

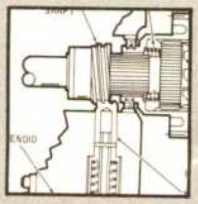

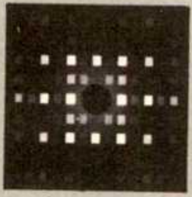

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NATURE Volume 244 • AUGUST 31 1973

Nuclear Defence: the need for Debate

A British Government document with extended discussion of the problems of Britain's future nuclear defence is a rare landmark A report of the House of Commons Expenditure Committee's sub-committee on Defence and External Affairs has just been published and contributes a valuable element to a debate on nuclear policy in the late 1970s and beyond—a debate which even now may peter out unless politicians, scientists and communicators continue to make sure that the public is well informed

The central question is not difficult to understand, however complex and equivocal the answer may be. In 1962, Britain purchased from the United States four nuclear powered submarines each capable of firing 16 Polaris missiles A Polaris missile can carry one megaton weapon or three devices of 200 kilotons each Although the triplet can split in flight to land in a pattern, it is not possible to tailor the patterns to individual target areas That is, present Polaris missiles are not multiple independently-targetable re-entry vehicles (MIRVs) A fleet of four submarines ensures that at least one boat is always on station The US operates forty-one such submarines There appears to have been general satisfaction both with the fleet's contribution to national security and its relative cheapness (about 1% of the Defence Budget goes in maintenance of the nuclear deterrent)

The question to be faced within the next year or two is whether to use the upcoming refits of these submarines to make any major modifications to their missile constituent Many options are open at the present and the choice has to be made on the basis of three considerations—political views on Britain's nuclear role in the world, military assessments of the nature of the defence which will have to be overcome and economic judgement on cost-effectiveness and the ability of Britain to pay for improvements The choices are as follows The missiles could be left as they are They could be MIRVed with British technology They could be replaced with the larger American Poseidon missiles, probably MIRVed (10 to 14 warheads in each of the 16 missiles, each warhead being 40 to 50 kilotons) Other more exotic weapon systems are further down the line and do not need immediate attention

The United States has refitted a majority of its boats with MIRVed Poseidon missiles but the United Kingdom should not automatically follow suit as the two countries have different defence needs Britain cannot plan to raise its nuclear arsenal up to a level at which it could consider demolishing either the whole Russian missile-launching capability or a large number of Russian cities, industries, dams and so on So it must work on a minimum deterrence posture—that in attempting to conquer Great Britain the Soviet Union would have to weigh the probable loss of a major city SALT has helped the British cause substantially since the restrictions on ABM sites make it likely that an attack on Moscow would at least inflict some damage, whereas trends in ABM development would otherwise have protected Moscow for the near future from the relatively primitive assault of Polaris missiles

The MIRVing of missiles is done for two purposes, to overwork ABM defences (which we have just seen are not going to be as good as they might have been) and to allow several targets such as individual missile silos to be attacked in a controlled manner Since a British nuclear force (used independently) would have to be used against a city to appear as even a minimum deterrent there thus seems little point in MIRVing the payload, whether it is Polaris or Poseidon

The Commons committee was in an almost impossible position when trying to view these issues from the financial point of view It is clearly not profitable to speculate too extensively on the economics of various options without knowing whether they make sense in political and military terms Thus the committee, led by the vigorous questioning of Dr David Owen, strayed almost continuously from its brief into attempting to understand the fuller picture This was the right thing to do in the circumstances as there is a desperate need for a public forum for the whole question

As it was, the evidence that the committee obtained was inadequate for the purpose of making anything approaching an economic assessment of nuclear options, but excellent for understanding the options themselves. Mr François Duchêne of the International Institute for Strategic Studies presented a lucid report on technological alternatives in the next ten years, although of course he was not in a position to do more than give order of magnitude guesses of the costs involved Mr Richard Garwin and Dr Donald Brennan submitted memoranda from the United States on technological and political questions of a British deterrent But the person from whom the committee should have expected the most specific evidence—Lord Carrington, Defence Secretary—turned in a performance which was unsatisfactory by any standard, and the committee let it be known that they were far from pleased Apparently the ministry's memorandum (not published) was mainly an essay on security and Anglo-US collaboration and in the words of the report "was not very informative on time scales and costs, nor on the various possible successors to the present systems" Neither did the Defence Secretary add much in his testimony The committee observed sourly "he also rather surprisingly said that he did not know the probable costs of the various options open to the Government"

On the basis of the evidence given, the committee was right to conclude that "there is a strong case for keeping the British strategic nuclear deterrent as it is", although it lacked anything like a detailed costing of the options There certainly should be no further scaling of the strategic ladder without an extensive debate on what is required politically and militarily, and this debate needs to be in public Alas, if the Ministry of Defence had their way public discussion would be frowned on because not all the facts would be available The ministry should look across the Atlantic and appreciate the virtues of informed external criticism and the amount of money it undoubtedly saved the American taxpayer when inflated internal demands for the best ABM defence that money could buy were met with detailed arguments from obviously competent outsiders The time is long past when defence issues, particularly those involving hundreds of millions of pounds, can be settled quietly within Whitehall by the armed services without external debate The results of a policy of excessive secrecy are clear in this report. The committee accepts, with little question, the conclusions of Messrs Duchêne, Brennan and Garwin because it lacks any counterbalancing view from Whitehall which thinks it is all too secret to talk about

It will be a matter of some surprise that the testimony came from two Americans and the director of an international institute Were there no British experts capable of enlightening the committee about their home country's needs? No British Brennans and Garwins, or for that matter Wiesners, Tellers and Rathjens? If not, this must be the result of a lack of flow of top level academics into and out of defence science and engineering Such flow would have the inconvenience for the ministry of fostering informed criticism but the virtue for the country of preventing stagnation of thinking within the ministry

Fortunately all is not lost for the scientist who would like to understand and participate in the debate on Britain's nuclear future A large number of the relevant facts are already widely known and published Beyond those facts anyone with intellectual curiosity can infer rather accurately the state of the art in defence hardware and software, and may even, by naively believing that defence thinking is always first-rate, be a year or two ahead of reality in his projections It is simply untrue to claim, as does Lord Carrington, that "unless one has access to the detailed knowledge which only the Ministry of Defence can have, I do not believe one will necessarily come to the right conclusions" Scientists have no end of case-histories to confound that sort of thinking Perhaps the Ministry of Defence knows it will get its way regardless and therefore cares little for this committee But if the community of those who are concerned for an effective and economical defence policy takes this recent encounter as a warning to do its homework and start independent thinking, the committee will have served its purpose

On the Right Road

THE British Association for the Advancement of Science has put itself through an exacting series of hoops during the past few years Only five years ago it was in deep trouble both financially and in its scientific vitality , now there are encouraging signs of life, as last week's meeting at Canterbury showed The constitution is new and slimmer, and under Sir Eric Mensforth's guidance as treasurer, the books balance

But what of the science? The BA has always had to look in two directions when presenting science—to the scientist to ensure fairness and accuracy and to the layman to ensure interest and comprehension As long as the annual meeting was the only occasion that the association was visible to most people, there was widespread feeling among both scientists and laymen that the BA was superficial When the expenditure of public funds on the BA was negligible, there was little that could be done about this, but now that there is an annual subvention from the government (via the Royal Society) of £20,000 change is necessary

It is thus most welcome that the BA is aiming for more visibility the year round At a press conference held during the meeting this year's President (Sir Kingsley Dunham) and Dr Magnus Pyke, the council's chairman, promised that the BA council would offer its opinions on scientific matters in the news as fast as it is able, although whether that will be fast enough for the daily press remains to be seen Furthermore in the past year the association has produced plans for its future activities which if they are fulfilled could see the association meeting a much felt need among British scientists

During the next year the association is to publish a number of "green papers" on items of current concern—for example on the funding of university research and on the ethical implications of trends in modern biology—and further studies on similar matters are promised The concern for a new role for the BA is not confined to Sir Kingsley and Dr Pyke , a number of the association's section presidents in their addresses see the BA as a forum where important matters of public interest can be studied and aired

How is this to be done? The answer lies in the appeal that the association is launching Companies and foundations are to be asked to sponsor particular activities of the BA, and these will include seminars and study groups on current issues The association declares itself willing to have commercial names linked to its work But it must be said that herein lies a danger The reason the BA is the ideal place for matters of public moment to be aired is that the association owes allegiance only to its members and to science. If its comments on environmental or other matters are to carry any real weight they must not merely be independent, but must be seen to be so

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100 Years Ago

THE additions to the Zoological Society's Gardens during the past week include two Persian Sheep (*Ovis aries*), presented by Mr. W. H. Shirley ; a Diamond Snake (*Morelia spilotes*) from New South Wales, presented by Mr. H. Frieland ; two Robben Island Snakes (*Coronella phocarum*), presented by the Rev. G. H. Fisk ; two Chubb (*Leuciscus cephalus*) and a Barbel (*Barbus vulgaris*) presented by Mr. E. S. Wilson ; two Ring-tailed Lemurs (*Lemur catta*) from Madagascar ; a King Parakeet (*Aprosmictus scapulatus*) from New South Wales ; a Black Cuckoo (*Eudynamys orientalis*) from India, purchased , a Weeper Capuchin (*Cebus capucinus* and a White-throated Sapajou (*C. hypoleucus*) from America, deposited.

From *Nature* 8, 372, August 31, 1873

OLD WORLD

Mellanby on the Decline of Science

by our Special Correspondent

Canterbury, August 24

AN attack on the organization of research, every bit as sweeping as was promised in the pre-meeting publicity, was delivered by Professor Kenneth Mellanby, Director of Monks Wood Research Station, at last week's British Association meeting in Canterbury Before the conference met Professor Mellanby promised to review the changes made since 1945 to improve research efficiency, to illustrate how they have almost all been counter-productive and to provide a solution And he did just that

Up to 1939, Professor Mellanby said, Britain received a good return from the money spent on research Now the return was a poor one The formation of research groups into rigidly organized teams, overstaffing of laboratories, the use of highly trained technicians and the appointment of the best scientists as administrative heads have all led to a decline Since 1938, Professor Mellanby said, overall government expenditure has increased twenty times but spending on universities has risen two hundred times and civil research expenditure some four hundred times But "I do not believe that there has been anything like a commensurate increase in scientific productivity, either in quality or quantity"

Professor Mellanby went on to attack the theory that there has been an information explosion Many new journals are review journals and "I do not think that the production of original research publications has more than doubled" Quality has not increased either "I see nothing to suggest anything other than fall-off in the appearance of work of exceptionally high quality in many fields of science"

Why has this decline occurred? "Success in original research depends almost entirely on the worker realizing the significance of his observations" Professor Mellanby said "In considering research I am therefore an uncompromising elitist—I believe that success and originality depend almost entirely on the efforts of a very few gifted individuals "

Up to 1939 professors and heads of departments produced large numbers of papers, now they may do no original research for years Departmental staffs are now five times larger and the best scientists are being sterilized by being used as administrators Rigidly organized teams, expensive recording equipment and the employment of highly skilled technicians are all counter-productive measures as the observations are now made by junior staff and not by the seniors who might realize the significance of what they see Nowadays senior staff only interpret other people's observations

The increased number of PhD students is also counter-productive, Professor Mellanby said Few theses resulted in original publications in spite of the "originality" of work theoretically required to obtain a doctorate, and far too much time was spent supervising PhD students Back in the 1930s, Professor Mellanby said, his supervisor, Professor Patrick Buxton, gave him less than 1% of his time

The lengthy reorganization of research that has followed last year's report by Lord Rothschild has been planned by people who in the 1930s would have been doing their most important research and "the new chief scientists appointed by the ministries would probably be better off giving vent to their ideas at a laboratory bench"

"My main worry about the situation is that it is one more unnecessary time-consuming complication which will produce a further host of unproductive administrators Already several previously productive scientists are spending hours, which they might have spent in their labs, wrestling with unnecessary and often bogus financial estimates "

So what is the Mellanby solution? His answer is simple Many of the staff currently in the research councils should be placed in development authorities while original workers should be identified and supported by the research councils in separate laboratories without too much expert assistance They should be given a three year contract and no security of tenure and allowed to get on with their work At any time the research worker could withdraw from original research and go to a development authority laboratory where the ideas generated by the research laboratories are exploited

"The next important change is to cut down the time spent on committee meetings A total ban on committees for a year would probably be a good first step, though a compromise with a few important ones meeting much less frequently would be more likely to meet with agreement" Committees should also prune themselves dramatically allowing those members with better things to do—in other words their own research—to resign first And administrators who are scientists should be allowed back to the laboratory bench

But while Professor Mellanby was planning to reorganize research so that the gifted few can give full time to their ideas, others were presenting the results of their efforts under the present system

Sir George Porter, Director of the Royal Institution, described how solar energy might meet future power demands, trials of a new drug—'Arvin'—which may prevent the recurrence of thrombosis were revealed, the dangers of computer dating, of tea-drinking while pregnant and of the repeated oil pollution of estuaries were postulated, and work on rheumatism that may lead to improved treatments was outlined

A symposium on Kent and Europe included a lecture by Dr I B Thompson of the University of Southampton which concluded that France had a great deal and Britain rather less to gain from the Channel Tunnel, while an industrial forum on the dangers of instability in our society due to scientific and technological advance failed to get to grips with its subject matter, and Hilary Rose traced the rise and fall of the British Society for Social Responsibility in Science

All in all the 1,500 who made it to Canterbury had rather better fare than last year, and the association plans to hold a meeting next year in Stirling where the projected symposia on Scotland and North Sea oil should show whether the association is a viable forum for the discussion of matters of public moment

In spite of the disappointingly small size of this year's meeting the association seemed very much alive and its plans to hold a student conference in January 1974, tied to the intention of giving both the students, and the school children who make up the British Association Young Scientists, a say in forming the section programmes in future, augur well

Dr John Kendrew is the president of the association which now has its new constitution A general committee of 59 members instead of 350 and a council of 22 instead of 75, aided and abetted by a full time council chairman is now in operation following the Privy Council's approval of the changes earlier this year

ANZAAS

Scientists Go Political

from a Correspondent

A COMPLETE and quite dramatic change in the relationships between scientists, the bureaucracy and the political world in Australia marked the recent 45th Congress of ANZAAS, the Australian and New Zealand Association for the Advancement of Science The Congress, held in Perth from August 13–17, was the first big scientific conference since the change to a Labor Federal Government last year

When the Whitlam Cabinet was formed in Canberra in December, several changes of significance to scientists were incorporated in the altered departmental structure, compared with the days of the Liberal/Country Party coalition which had governed Australia for the previous 23 years These were strikingly reflected at the Congress

Before last December, the only federal government department involved directly in scientific activity was the Department of Education and Science , its major effort was in education The Labor Government split this in two, thus providing a separate Department of Science for the first time, although it should be added that this department, like a number of others, is controlled by a Minister with more than one portfolio (the Minister for Science is also Minister for External Territories, the latter task demanding much of his attention as Papua–New Guinea approaches self-government) New Departments of Environment and Conservation, and Urban and Regional Development were also created, largely as a result of extensive consultations between the Labor Party, when in opposition, and the scientific and academic communities

ANZAAS is comprehensive in its coverage of academic disciplines Ever since its first Congress in 1888, it has included non-scientific and semi-scientific subjects like history, anthropology, economics, education, sociology, architecture and town planning and psychology Consequently, the ANZAAS Congress was an excellent testing ground for evaluating the extent to which the academic and research communities of Australia, on the one hand, and the political and bureaucratic structure, on the other, are getting on with each other under the new government

In contrast with the Liberal/Country Party days of power, when relations between science and politics were marked by antipathetic philosophies and some mutual suspicion, the many Labor politicians who came to ANZAAS fitted easily into the scene, delivering papers in their own right, and participating freely in discussions on contentious issues The Federal Ministers of Science, Environment and Conservation, Social Security, Immigration, Education, and Urban and Regional Development were all on the list of speakers Several ministerial advisers and departmental heads also took part (both of these groups in Canberra now contain a significant number of scientists for the first time) Extensive, open discussion and lobbying with politicians and their staffs were features never previously observed at an Australian science conference This was particularly timely in that the Congress preceded by a few days the handing down of the first Labor budget, in a Parliamentary session which will include many measures of importance to science and technology

The ANZAAS organizers defined the congress theme as "Science, Development and Environment" Each afternoon was devoted to three major symposia on variations of this theme, with a considerable degree of overlap This is illustrated by the titles of some of the symposia "The Scientists, the Bureaucrat and Environmental Responsibility" "Limits to Growth Population in Australia", "Resource Management and Planning", "Education and Environment", "The Implications of Nuclear Explosives", "Whither Urban Australia?", and "Ord River Ecology" It was in these symposia that most of the political content was included The largest press, radio and television corps in ANZAAS history backed up by excellent facilities made sure these aspects were widely reported

On the campus of the University of Western Australia the 2,900 professional delegates were joined by a record 2,300 students Secondary school students were given leave to attend the Congress and this younger generation was active in questioning speakers, notably in the smaller sessions Eight hundred and fifty papers were delivered in 24 different specialist sections Although New Zealand is meant to be an equal partner in ANZAAS, there were few delegates from that country, whose capital Wellington is roughly as far from Perth as Sverdlovsk is from London It was inevitable, then, that those scientific developments which received attention were related virtually exclusively to Australia

CEREALS

Shorter Wheat

A FEW weeks ago there was great consternation that this year's wheat crop in Britain had been ruined by high winds But fortunately the good weather and abundance of sunshine recently, combined with the fact that the wheat was nearly ready for harvesting anyway, has ensured that most of the crop was saved It could well have been a different story if the past two weeks had been wet and stormy

Cereal crops can still be harvested after they have been partially flattened by winds or rain but if the crop is flattened early in the summer before the cereal is ripe then the erect crop ripens before the flattened cereal, which causes difficulties at harvesting time Another difficulty with flattened cereal is that weeds are much more likely to grow through and smother the crop, resulting in loss of yield But of greater importance, the laid crop will not be of the best quality

Clearly it would be of great advantage to the farmer if the cereal was less prone to flattening by winds and rain and, in answer to this, one of the aims of plant breeders is to produce cereal which has either a stiffer straw or one which has a shorter straw—the so called dwarf cereals The farmer has another purpose in demanding short stem cereals, and that is that nowadays farmers do not need as much straw as they did several years ago Chemical fertilizers have now mostly replaced farmyard manure for which straw was neded

There is little doubt that in the coming years dwarf cereals will gradually replace the longer stem varieties But dwarf varieties of wheat, in particular, have some way to go before they can match the longer stem varieties in yield, quality and resistance to disease

The grain of dwarf varieties of wheat at present being tested in national trials is soft milling and of a poor bread making quality Most of the wheat used for bread making in Britain comes from overseas

During recent years, however, more and more of the softer British wheat has been used in making bread of an acceptable quality because of improved milling and baking techniques Even so about two-thirds of British wheat is still used for animal feed or for making biscuits

Another difficulty with dwarf wheats is that control of tall weeds may be more difficult than it is with longer stemmed varieties Some grass weeds in wheat fields are controlled by spraying with chemicals but it has been found that many of the dwarf varieties like some of the taller wheats are readily damaged by these chemicals But it is possible that the early vigour of many dwarf varieties will provide an environment in which most weeds will fail to grow

It is also possible that short stem wheats will be more susceptible to *Septoria* leaf- and glume-blotch because the shortness of the stems could lead to a humid environment conducive to the development of these diseases It has been suggested also that spread of disease by rain splash will be easier in the short stem varieties

NEW WORLD

Publishers step up Fight against Photocopying

by our Washington Correspondent

A LEGAL and legislative battle, the outcome of which will have important implications for the scientific community, is taking place in the United States over copyright At issue is the right of libraries to provide researchers with photocopies of published material, such as scientific articles And, according to some publishers, the survival of specialist journals is also at stake

The matter has been brought to a head recently by two separate developments, the first of which is a court case brought by a publishing company against the National Institute of Medicine, and the second is a bill to amend the 1909 Copyright Act, which is under consideration by a Senate subcommittee In general, the battle lines are loosely drawn between publishers on the one hand, who are concerned that extensive photocopying of journal articles will cut into subscriptions, and libraries and their clients on the other, who are anxious that harsh enforcement of the copyright laws will stifle research and cripple the interlibrary loans system by which resources are shared between libraries

The court case was brought last year by Williams and Wilkins Co , a publisher of some 37 medical journals including the *Journal of Immunology* and *Medicine*, who charged that the National Library of Medicine and the library of the National Institutes of Health, had infringed the copyright laws by providing photocopies of journal articles to scientists and to other libraries Their suit, the first judicial review in more than 60 years of the so-called "fair use" provision of the Copyright Act, was filed in the US Claims Court, a special court for claims against the federal government

The publishing company won the first round on February 16 when Comissioner James F Davies ruled that the libraries had been photocopying on such a large scale that they had indeed infringed the copyright laws But the government has appealed the case, and it is expected eventually to end up in the US Supreme Court

Meanwhile, on Capitol Hill, a bill introduced into the Senate by Senator John McClennan of Arkansas and under consideration by his subcommittee on Patents, Trademarks and Copyrights, is providing another battleground Designed to bring the 1909 Copyright Act into the age of broadcasting and global communications, the bill contains a "fair use" provision which would allow individuals to make copies of copyright material for such purposes as criticism, news reporting, teaching, scholarship and research In deciding what constitutes fair use, the bill suggests that such factors as "the purpose and character of the use, the nature of the copyrighted work, the amount and substantiality of the portion used in relation to the copyrighted work as a whole, and the effect of the use on the potential market for or value of the copyrighted work" should be taken into account But it also contains a provision which would severely limit the right of a library to make a photocopy of copyrighted work It is that provision which is being fought tooth and nail by educational and library organizations

In short, the provision would allow a library to make a copy of such material only if it is satisfied that the work could not be obtained through the usual commercial channels In other words, no library would be able to photocopy an article from a scientific journal which is still in print and available at the usual price, without paying royalties to the publisher McClennan's subcommittee recently held two days of hearings on the bill, at which there was a considerable clash of opinion

Representatives of library associations and educational organizations argued that the provision would place an intolerable burden on library resources and that it would hamper scientific research They pointed out that it would involve considerable work on the part of library staff to determine whether the material was readily available, and that the necessity for paying royalties would, in the words of Stephen McCarthy, Executive Director of the Association of Research Libraries, "cost dimes to collect pennies"

But those who oppose the restrictions are particularly concerned that they would cripple the interlibrary loans system The system often works by a student or researcher requesting a journal article from one library, which obtains a photocopy for him from a different library Clearly, the system holds particular benefit for small libraries which cannot afford to carry vast stocks of journals

Publishing companies are, however, greatly concerned about the growing use of photocopying in general, and the interlibrary loans system in particular Kenneth Keating, the new US Ambassador to Israel, who was testifying at the hearings for Harcourt Brace Jovannovich Inc , and Macmillan Inc , summed up the situation like this "as reprographic technology progresses, interlibrary affiliates grow, and information transfer systems develop, educational and trade publishers are likely to find the economic realities of their businesses approaching prohibitiveness" And Arthur J Rosenthal, Director of the Harvard University Press, said "the journal publisher finds himself unable to pass on higher costs to the consumer, who at some point in the scale will prefer photocopying to subscribing"

But all the publishers were adamant that they do not want to put a stop to photocopying entirely—all they want is some compensation in the form of royalties Robert Cairns, Executive Director of the American Chemical Society suggested, for example, that publishing costs should be shared by the users, which is not the case if unrestricted photocopying is allowed In support of his claim that publishers are suffering from the increase in photocopying, Cairns said that in the past three years, circulation of the *Journal of the American Chemical Society* has declined from 19,419 to 16,139, and that in the first six months of this year, it has dropped even further, to 14,726

If the publishers' arguments eventually persuade Congress to pass the copyright bill, how could a system be devised for collecting royalties which would not cost more than it brought in? One answer may lie in the bill itself, which would set up a National Commission on New Technological Uses of Copyrighted Works to study such matters But the Williams and Wilkins Co believes it may have a solution to the problem The company has proposed charging a higher price to libraries than to individuals, and the extra payment would entitle the library to provide single photocopies of articles to individuals Such an arrangement would not, however, allow the libraries to make photocopies for other libraries in the interlibrary loans system, but Mrs A Albrecht, an official of Williams and Wilkins, said last week that the company is now considering a three tier price structure for its journals—those libraries which wish to provide copies to other libraries would pay an even higher price

There is one argument against the restriction on photocopying by libraries which may prove to be particularly telling, however It was pointed out that it would prevent members of Congress and their staff from receiving photocopied material from the Library of Congress and the Congressional Research Service, unless they would be willing to pay the royalties

PHARMACEUTICALS

Librium and Valium

by our Washington Correspondent

It has been a bad year for the giant Swiss pharmaceutical firm, Hoffmann–La Roche, and its two biggest money spinners, Librium and Valium Under fire from authorities in Britain for allegedly making vast profits by overcharging the National Health Service for the two tranquillizers, and under investigation in Brussels for charging widely differing prices for Librium and Valium in different European countries, the firm received a new setback from the US government recently The Drug Enforcement Administration, the new Federal agency concerned with drug abuse law enforcement, proposed that the two drugs should be placed under tighter control because of their potential for abuse

The action ends a seven-year legal battle between the government and Hoffmann–La Roche over the need to regulate more tightly the prescribing and manufacture of the two tranquillizers In short, Mr John Bartels, the Acting Administrator of the Drug Enforcement Administration, has urged that Librium and Valium be placed on Schedule IV of the Controlled Substances Act, a move whose chief effect will be to limit to five the number of times a prescription for either drug can be refilled , at present, doctors can write prescriptions for the drugs which can be refilled any number of times The proposed regulations can hardly be described as burdensome, however, and their chief result is likely to be to make doctors more conservative in their prescribing habits and the public more cautious in taking the drugs Some such education is clearly needed

Even by American standards Librium and Valium are swallowed in staggering amounts in the United States According to the Drug Enforcement Administration, 12 tons of Valium and 10 tons of Librium were prescribed last year, which is sufficient for about 20 capsules for every man, woman and child in the country The two tranquillizers are reckoned, in fact, to be the most heavily prescribed drugs in the United States

As for their abuse potential, however, officials in the DEA admit that the drugs do not pose as great a problem as barbiturates and amphetamines, for example, but the National Commission on Marihuana and Drug Abuse reported earlier this year that about 6% of US adults and 3% of youth have used minor tranquillizers for self-defined purposes The drugs have also been reported to cause physical and/or psychological dependence, resulting in the withdrawal symptoms of insomnia, nausea, agitation, twitching, sweating and convulsions after prolonged use of high doses

The proposal to bring Librium and Valium under the Controlled Substances Act is now being studied by the Food and Drug Administration, but no opposition is expected Hoffmann–La Roche had fought the proposal in the courts, but has now agreed to withdraw its legal action

EDUCATION

Graduate Students Fewer

by our Washington Correspondent

The number of students taking graduate courses in science and engineering at US universities declined last year for the third year in succession According to figures published by the National Science Foundation, keeper of the federal government's statistics on science and technology, first year enrolments in graduate science departments dropped by almost 3% from 1971 to 1972 Every branch of science except for the life sciences reflected the drop, with engineering showing the largest decline, 5%, and physics not far behind with a reduction of 4% in total enrolments In contrast, the number of students enrolled in graduate courses in the life sciences remained almost static

The decline can be explained chiefly by large cutbacks in federal support for graduate students , in particular, graduate support provided by the National Science Foundation and the National Institutes of Health has been chopped in the past few years The figures show, for example, that the total number of students directly supported by the federal government dropped by 10% between 1971 and 1972, with the life sciences again showing the smallest decline, 6%, and mathematical sciences the most affected, declining by 20%

But, while graduate student enrolments in the sciences have been decreasing, postdoctoral appointees have been on the upswing—their numbers increased by 86% from 1971 to 1972 That trend, the NSF suggests, is "an indication that the tightening of the job market for PhDs in industry, higher education and government resulted in the absorption of more postdoctorals into graduate science education programs than ever before" The NSF's figures are based on a survey carried out in the autumn of 1972 of all US colleges and medical schools granting PhD degrees

IMMIGRATION

Brain Drain Slows

by our Washington Correspondent

Early in 1971, the federal government tightened up its immigration regulations, by stipulating that aliens could work in the United States only if they have a job offer for which domestic workers are not available and if their employment does not affect domestic wages and working conditions The effect of the regulations on the brain drain has been significant According to figures released last week by the National Science Foundation, the number of immigrant scientists and engineers admitted to the United States in fiscal year 1972 dropped by 14% compared with 1971 In absolute terms, 11,300 immigrant scientists and engineers were admitted to the United States in 1972, 13,100 in 1971, and 13,300 in 1970—the peak year The most marked decline has been in the field of engineering, and the figures also reveal that 70% of all scientists and engineers who entered the country last year were born in Asia

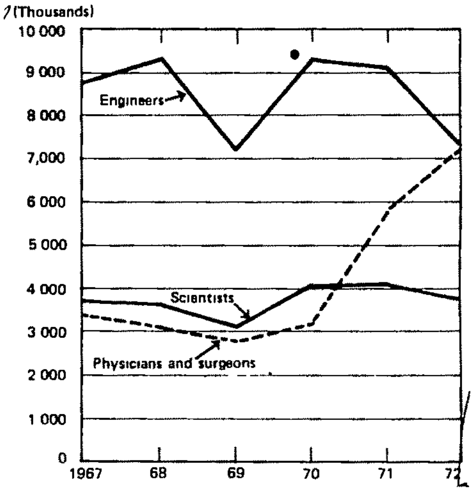


Fig. 1. Immigrant scientists, engineers, physicians, and surgeons, by broad occupational group, FY, 1967–72 *

*Source National Science Foundation

In contrast, the number of immigrant physicians and surgeons admitted to the US in 1972 jumped to 7,100, from 5,700 the previous year In the past, no more than 3,300 physicians and surgeons entered the US in any one year The reason for the rapid increase in numbers is that there is a shortage of personnel in the domestic medical profession, and so immigration restrictions are not so stringent It goes without saying, however, that many of the physicians and surgeons who come to practice in the US leave countries where the shortage is even greater

NEWS AND VIEWS

Preponderance of Theories of Gravity

THE only precise tests of the applicability of the theory of general relativity to the actual physical world are those long ago proposed by Einstein, and certain other tests proposed more recently that are closely related to Einstein's All these tests are confined to laboratory experiments or astronomical observations within the nearer parts of the Solar System They test the theory only to the so-called post-Newtonian approximation, roughly speaking to terms in $1/c^2$, where c is the speed of light No observation has been found to contradict the theory to this approximation There is always a possibility, however, that new non-relativistic phenomena will be discovered (such as a fast rotation of a central part of the Sun that could lead to an effect upon the perihelion motion of the planets, about which conjectures have from time to time been made) that may necessitate a revision of the effects to be compared with the predictions of relativity theory In that case it might have to be recognized that general relativity would not agree with observation in the post-Newtonian approximation A well-known modification of general relativity introduced by C H Brans and R H Dicke for a somewhat different reason does give a different post-Newtonian approximation and it, as an example, might some day be found to agree with observation better than general relativity

As regards more general tests, general relativity apparently gives a qualitatively satisfactory account of gravitational collapse and the phenomenon of black holes, but no quantitative tests have yet proved possible It has led to a highly developed treatment of gravitational waves, but there is no general agreement about the significance of such observational tests as have so far been attempted Also general relativity may be said to give a qualitatively acceptable treatment of cosmological models, but the observational situation is complicated and obscure General relativity may be regarded chiefly as a theory of the gravitational field Attempts to extend it to include electromagnetism and other fields have met with little success in principle, and none at all in predicting new observational phenomena.

Such, in crude outline, seems to be the current state of the comparison of observation and theory in general relativity It is disappointing Probably few physicists would seriously doubt that general relativity provides the best theory of gravitation we possess But probably also all physicists expect that the possibilities of measuring times and distances with the astonishing precision now attainable, the possibility of studying the effects of the so-called curvature of space out to the distances of the most remote quasars, the possibility provided by neutron stars and pulsars of studying the effects of gravitational fields about a million times more intense than any known before, as well as other new techniques and phenomena, will soon transform the situation as regards observational tests

The recent publication of an article on certain aspects of the subject, under a mischievously provocative title (Wei-Tou Ni, "A New Theory of Gravity", *Phys Rev*, **D7**, 2880, 1973), is a reminder of one particular group of relativists who have been keeping the situation under sophisticated professional review This group at California Institute of Technology is led by Professor Kip S Thorne During the past few years, recent members of the group, chiefly C M Will, K Nordtvedt and Wei-Tou Ni, have produced a substantial series of articles in the *Astrophysical Journal*, and elsewhere, in which they exhaustively classify theories of gravitation in a well-defined category, to which general relativity and the Brans-Dicke theory belong, and systematically analyse the possibilities of observational test Evidently they hoped it might emerge that existing tests might already rule out theories in the category other than general relativity itself (or any theory that reduces to it for a suitable choice of parameters) They seem further to have conjectured that general relativity might be unique in the category at the level of the post-Newtonian approximation

The "new theory" is simply a counter-example that invalidates these conjectures It is a theory within the category that is shown to agree with all experiments to date, that for suitable values of its adjustable parameters has exactly the same post-Newtonian approximation as general relativity, and that nevertheless never reduces to general relativity in full In the academic context, it is a considerable technical feat to have produced such an example Presumably the chief lesson we are intended to draw at this stage is that existing experimental tests are less conclusive than they are commonly supposed to be

The new theory is much more elaborate than general relativity, it involves four auxiliary gravitational fields (one tensor, one vector and two scalar) from which the physical metric tensor is generated by a complicated process, and it is found to involve four arbitrary parameters As Ni remarks, there are important features of the theory that he has not yet studied, notably its ability or otherwise to produce cosmological models

General relativity is thus very obviously distinguished from the new theory—and all others in the category—by its relative simplicity Pure general relativity (without the cosmic constant) contains no adjustable, or "universal", parameter (Speed of light and the gravitation constant G are no more than conversion factors which appear only if units of measurement are prescribed in advance) Thus, general relativity in this form seems to tell us about the way in which we can describe our experience of the physical world In so far as the distinction is significant, it does not tell us about what the world is made of, for this would presumably require the intervention of physical constants The most significant thing about the gravitation field seems to be that it makes its appearance at this very rudimentary stage of physics Gravitation seems not to depend upon any particular properties of matter, for these must require physical constants to specify them If this is truly significant, then the new theory of gravity that does involve adjustable parameters would not be expected to give fresh insight into the nature of gravity itself so much as telling us how other fields might be affected by gravitation It is much to be hoped that the classification of theories will be interpreted from this standpoint

W H McC

Meteor Spectra and Meteoroid Composition

VISUAL meteors, or to give them their colloquial name, shooting stars, are produced when an interplanetary dust particle of mass greater than 0 1 g collides with the Earth's atmosphere and burns up These particles are in the main porous, crumbly objects composed of loosely conglomerate sponge-like material and have geocentric velocities of about 130,000 km h^{-1} The surface temperature of the meteor soon reaches boiling point as it collides with and adsorbs air molecules, and in this state the impacting meteor is eventually reduced to its constituent atoms by sputtering and ablation mechanisms The available kinetic energy is dissipated as an atomic and molecular excitation spectrum, as continuous thermal radiation, as a dense ($>10^{15}$ m^{-1}) column of electrons along the meteor path and finally (and principally) as heat Less than 0 1% of the energy appears as visual luminosity

One of the more pressing problems of meteor science is the detailed analysis of the composition of these dust particles Obviously they cannot be collected by sounding rockets because the relative velocity is so large that they are completely destroyed on impact with the collecting surface Only two paths remain open, one being the spectroscopic study of the resulting visual meteor, the other being the mass spectrometric analysis of the atmosphere in the meteor region (heights between 75 and 105 km) using rocket-borne spectrometers

The typical meteor spectrum is one of low excitation, with the ionization potentials of the ions lying in the range 1 9 to 13 9 volts—this being equivalent to a temperature range from roughly 1,680 to 4,800 K The upper state population is of the order of 10^{15} to 10^{17} The following elements are observed in the spectra of the meteor head neutral atoms FeI, MgI, NaI, CaI, MnI, CrI, AlI, NiI, HI, OI, NI, ionized atoms CaII, MgII, SiII, FeII, NII, OII Furthermore, CoI, SrI, SrII, BaI, BaII, SiI are sometimes identified but their presence is doubtful The meteor spectrum changes with the velocity of the particle and the luminosity of the meteor, the CaII lines H and K being the main feature for fast meteors and NaI, MgI and FeI being dominant in the spectra of slow meteors The evanescent train for fast meteors shows a much lower excitation level than the meteor head and in general there is an absence of ionized lines These trains (or wakes) often contain molecular lines of, for example, N_2, FeO, MgO, CaO, CN, C_2, CO and CO^+

By applying the emission curve-of-growth method to meteor spectra of high dispersion the spectra can be quantitatively analysed This has been done by Ceplecha (*Bull astr Inst Czech*, **17**, 195 , 1966) for two spectra from slow meteors and the computed elemental abundances are approximately those of an average stony meteorite Problems arise with this method because the excitation temperature, an important parameter in the calculation, varies as a function of the length of the luminous volume It is thus very difficult to construct the emission curve of growth for optically thin lines

The problem of determining the element abundance of meteors from their spectra is re-examined by Harvey (NASA, Langley Research Center) in the *Journal of Geophysical Research* (**78**, 3913 , 1973) Harvey tackles the question of self absorption in the meteor plasma in two ways , first, by comparing the spectral photometry used in the data reduction with spectrograms which indicate optimum self absorption and, second, by comparing the observed radiant energy with that expected from an optically thick plasma He concludes (contrary to the finding of Ceplecha (*IAU Colloquium*, **13**, NASA SP 319, 1973)) that there is negligible self absorption in most optical meteor trains Ionization in the train, however, does affect the optical radiation because it leads to neutral atom depletion and it must therefore be considered when calculating the elemental abundances The effect is significant for the lower ionization potential elements (Na, Ca) but negligible for elements such as Fe, Ni, Si and Mg It is interesting to note that neutral atoms are depleted not only by ionization but also by the incomplete dissociation of stable molecules

Harvey has analysed the spectra of five meteors in detail and the results indicate that the incident meteoroids have elemental abundances similar to those of carbonaceous chondrites, the uncertainties in the abundance determinations depending directly on the ionization and dissociation corrections The analysis was checked by using a sample of the type 3 carbonaceous chondrite Allende, a stony meteor which fell in Mexico in 1969 This produced a comparison meteorite spectrum of known chemical composition Using a dc arc as an excitation source Harvey found that the meteorite spectrum was very similar to that of Taurid and Geminid meteor spectra previously obtained by him Another heartening conclusion was that the elemental abundances of Allende obtained from the spectra were in good agreement with those obtained chemically Harvey found that of the meteor spectra analysed most indicate that the incident meteoroids have compositions similar to carbonaceous chondrites

Meteoroids are the solid dust particles of cometary nuclei which get pushed away from the nucleus by gas pressure produced by the sublimation of the volatile cometary ices Harvey's work therefore supports the generally accepted conclusion that cometary dust is primaeval, being made up of the primitive solid essence of the condensing nebula that formed the Solar System Also about 99% of cometary dust and meteoroid particles are found to have the same composition, which is similar to the elemental composition of carbonaceous chondrites

Thus the considerable variations found in the densities of meteoroids in different meteor streams and also in the sporadic background (for example, 2% of the sporadic meteoroids have been found to have an original density of 6 6 g cm^{-3}, 4% 3 4 g cm^{-3}, 10% 1 5 g cm^{-3}, 46% 0 4 g cm^{-3} and 38% 0 05 g cm^{-3}) must be due to physical and not chemical causes

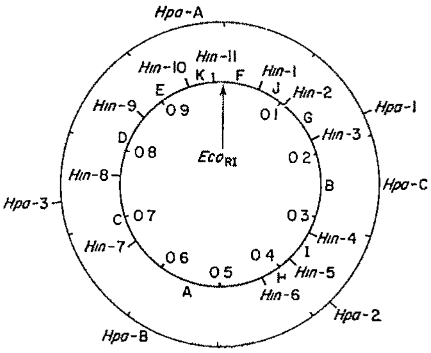
D W H

Dissecting SV40 DNA

BY comparison with the sophistication of bacteriophage genetics, the genetics of eukaryotic viruses is still a very green field It is rapidly maturing, however, with recent studies on SV40 and polyoma virus, spurred by the hope that the genetics of these transforming viruses may elucidate the mechanism of neoplastic transformation

Fortunately, the size of the SV40 genome (3×10^6) makes molecular dissection manageable, although smallness is a disadvantage for other reasons It is the attribute of small size and the availability of certain enzymes which allow analysis by specific digestion followed by isolation of the resulting small number of fragments—a procedure which would be daunting with large molecules. Specific fragments can be ordered, and so a form of molecular map can be made, regardless of whether anything is known about the nature and extent of individual genes Provided that the fragments produced in the first place are of a size suitable for specific molecular hybridization and that RNA products of the genome in question are available, then information will be obtainable about individual genes

Two recent papers together go far towards complete functional analysis of the SV40 genome First, Danna, Sack and Nathans (*J molec Biol*, **78**, 363, 1973) report their construction of a complete cleavage map by a meticulous and exhaustive analysis of the fragments produced by treatment with bacterial restriction enzymes In the following paper, Khoury, Martin, Lee, Danna and Nathans (*ibid*, 377) use the SV40 fragments to analyse the origin of the viral RNA molecules transcribed during lytic infection of African green monkey kidney cells (BSC-1)



Cleavage map of the SV40 genome

The method used to obtain a cleavage map was chosen because the R_I restriction endonuclease of *Escherichia coli* (Eco_{RI}) breaks SV40 DNA at one site only, whereas the restriction enzymes from *Haemophilus influenzae* and *H parainfluenzae* break it at eleven and three sites respectively The resulting fragments can be separated from each other on polyacrylamide gel slabs—so providing, simultaneously, information about their molecular weight and therefore about the proportion of the total genome which they represent

In a manner analogous to the sequencing of a protein molecule, Danna *et al* obtained a series of overlapping fragments, so as to deduce the order of their limit products, and emerged with a map (see figure) Map distances are in relation to the Eco_{RI} cleavage site The existence of this map means that specific pieces of SV40 DNA can be used as probes to select those RNA molecules which are complementary to them within a given population of cell RNA Having selected viral RNA molecules, it is a comparatively short step to deciding what is the relation between the restriction fragments and individual genes

Khoury *et al* are concerned with the achievement of both these aims Not only have they discovered which and when sections of the SV40 genome are transcribed during lytic infection but, also, they have determined the position in the cleavage map of the "early" and "late" template regions, and the direction of their transcription. SV40 DNA molecules labelled with ^{32}P were cleaved by *H influenzae* restriction enzyme, complementary RNA molecules were selected from "early" or "late" total RNA by hybridization, and the resulting hybrids were isolated by hydroxyapatite chromatography

The results confirm that early transcription is from the minus strand, and in addition show that it involves four of the eleven restriction fragments (A, B, H and I) Late transcription is from the plus strand and involves fragments C, D, E, K, F, J and G, parts of A and B, and probably also of H and I Presumably, fragments A, B, H and I contain sections of different genes, although the authors cannot say precisely which regions of them are transcribed from the plus and which from the minus strand As to the direction of transcription, establishment of the 3′ to 5′ orientation of DNA strands within the cleavage map is sufficient Khoury *et al* show that early transcription is counter-clockwise from A to B, and late transcription is clockwise from A to B Predictions can, furthermore, be made about the position of initiation and termination sites A similar analysis of SV40 transcription in transformed cells is under way

Something is already known about the function of the RNA products coded for by SV40 DNA, for example, the region of the genome which is transcribed early in lytic infection is required for expression of U and T antigens, and of the SV40 tumour specific transplantation antigen It cannot now be long before the limits of these structural genes are defined, or, indeed, before even their nucleotide sequences are known The information that this will provide may be of value far beyond the confines of one small DNA virus

From a Correspondent

VITAMIN C

For and Against

from a Correspondent

A CONFERENCE on vitamin C and the common cold organized at Stanford University on August 6 and 7 on behalf of the Departments of Chemistry and Chemical Engineering by Professor Linus Pauling (Stanford University) provided a timely review of the current controversy on the therapeutic value of high intake of ascorbic acid and some new data The opposition of the medical profession to the use of mega quantities of ascorbic acid—in contrast with the much smaller amounts acknowledged as necessary for prevention of scurvy—is well known Evidence based upon double-blind trials was presented by several speakers to show that high intake of the vitamin, although not necessarily decreasing the numbers of colds, favours decrease of their severity

Professor A Szent-Gyorgi (Marine Biological Laboratory, Woods Hole) traced the history of his discovery and isolation of L-ascorbic acid—for which he was awarded a Nobel prize in 1937—and accused the medical profession of being blind to the results of double-blind trials Dr I Stone (University of California) outlined his original idea of hypoascorbemia in terms of a gene deficiency, discussed in more detail in his recent book, on *Vitamin C and Disease* Professor Pauling marshalled numerous cases favouring the concept that a dosage of several grams of vitamin C rather than the accepted 100 mg dosage is required each day

Research on the metabolism of vitamin C was discussed by Dr J J Burns (Hoffmann-La Roche, Nutley), man metabolizes ascorbic acid at a considerably slower rate than the guinea-pig —with respective half lives of 15 days and 3 days—which may explain why guinea-pigs develop scurvy more rapidly Certain chemicals including barbiturates and 3–4 benzpyrene which stimulate ascorbic acid biosynthesis in the rat also inhibit markedly the activity of oxidative enzymes in liver microsomes which detoxify the drugs The vitamin also interferes with the reaction of nitrites and secondary amines to form nitroso derivatives, which may be carcinogenic in certain animals Dr L Spero (University of Toronto) outlined several of the problems of research into the pharmacological effects of high doses of ascorbic acid and reviewed methods for assaying total ascorbic acid and dehydroascorbic acid content

The prophylactic uses of doses in excess of 1 g daily of vitamin C were considered in detail by Dr J Coulehan (Lower Greasewood Indian Health Center, Arizona), Dr R Colby (Stockton State College, New Jersey), Dr T Chalmers (National Institutes of Health, Bethesda) and Dr T W Anderson (University of Toronto) Their experiences differed somewhat because considerable individual variations were recorded Although in some cases a trend towards freedom from attack was noted, a more common effect was a reduction in the severity of colds Some concern was expressed about the proportions of interchanges of tablets between patients and about the extents of reliability on the types of placebo tablets The problem of bias in the results was also considered by Professor D M Hegsted (Harvard University School of Public Health, Boston), and Professor R Hodges (University of California, Davis) considered that the available evidence cannot be taken as unequivocal in favouring the intake of mega quantities of the vitamin Disquiet was expressed by more than one speaker, in particular Professors Pauling and Szent-Gyorgi, about reports that tablets for large doses of vitamin C may be banned in the United States

The effects of vitamin C on viruses were considered by Professor T Merigan (Stanford University School of Medicine) , some viruses are susceptible within a short time to the presence of ascorbic acid, compared with HCl, whereas others are hardly affected Dr S Lewin (North East London Polytechnic, London) suggested physicochemical explanations for some of the results obtained with vitamin C, proposing that the interfacial tension of water may be reduced (which may account for the influence of ascorbic acid on viral organization) and that ascorbic acid may break down in aqueous solution Some of the negative results obtained in ascorbic acid trials might be due to the proportion of ascorbate salt used, leading to inactivation *in vivo* The difference in *p*H between the stomach and duodenum may be important in this reaction

Concluding the conference, Professor Pauling re-evaluated available data, including those presented in his book on *Vitamin C and the Common Cold,* and considered them to be in favour of the thesis that mega quantities of vitamin C are beneficial The forum provided at the conference for both proponents and opponents of the use of mega quantities of the vitamin prompted a useful evaluation of available data

POPULATION ECOLOGY

Evolutionary Stability

from our Animal Ecology Correspondent

FOLLOWING hot on the heels of Maynard Smith and Slatkin's paper on stability in predator–prey interactions in vertebrate animals (*Ecology*, **54**, 384 , 1973), comes an equally pleasing one from van den Ende on the ecological and evolutionary relations at work within continuous culture systems of invertebrate carnivores and their prey (*Science*, **181**, 526 , 1973) When Gause carried out his now classic experiments on the dynamics of mixed populations of *Paramecium* and *Didinium*, he reinoculated his cultures every 3 or 4 days to prevent elimination of one or other of the species The result was a series of quite violent oscillations It has been estimated that about 65% of the *Paramecium* would have had to be saved from predation for stabilization of the system

Van den Ende established cultures in glass culture dishes of the protozoan *Tetrahymena pyriformis* which feeds on the bacterium *Klebsiella aerogenes* The physical environment was held constant, so ensuring that fluctuations in population density were only the result of interaction between the two species During the 1,000 hours following the introduction of the predators among their prey, five oscillations in bacterial density were observed , each was shadowed by an oscillation in protozoa density Towards the end of the time period the frequency and amplitude of the oscillations became less and it seemed that some degree of balance had been achieved The fascinating aspect of this work is precisely how this equilibrium came about

According to Gause's "Principle of Competitive Exclusion", no two species can share the same ecological niche Therefore, unless two niches had been available in van den Ende's seemingly homogenous environment, one species should have become extinct, as one invariably did in Gause's experiments It seemed, however, that the walls of the glass culture vessels provided sufficient heterogeneity to allow the co-existence of the two species

A rapid increase in the number of bacteria between 150 and 200 h following introduction of the predators was marked by the disappearance of polysaccharide capsules around the bacteria and the appearance of non-capsulate colonies Non-capsulate colonies stick to glass very well and require a force of 10^{-8} dynes (when the culture is stirred at 300 revolutions per min) to dislodge *Tetrahymena* is a ciliary feeder and is unable to increase its feeding currents to that extent Thus once on the wall of the vessel a prey item is relatively inaccessible to the predator, and it can be said to have occupied a different ecological niche from its fellows still at large in the liquid phase When bacteria from the walls of the experimental culture were placed in control vessels they showed a marked preference for growth on solid surfaces and in large non-capsulate aggregates Thus it seemed that a genetic change of fundamental importance to the bacterial population had taken place as a direct result of its exposure to predation

Predatory organisms are under constant evolutionary pressure to become more skilful at prey catching, and prey are under a similar pressure to become more evasive Natural selection, in allowing a certain number to be eaten, thereby maintaining the system, favours

Lepore and Anti-Lepore Again

STUDIES of the two unusual human haemoglobin variants, Lepore and anti-Lepore, continue to provide information on the details of protein biosynthesis It will be recalled that the non-α chains of Lepore haemoglobins are $\delta\beta$ fusion chains, formed as a consequence of homologous but unequal crossing-over of the δ and β-chain genes In Lepore haemoglobins the N-terminal segment is derived from the δ chain, whereas in the anti-Lepore variants the N-terminal segment is part of the β-chain sequence

In *Nature New Biology* next Wednesday (September 5) Roberts, Clegg, Weatherall and Ohta report that the $\beta\delta$ chain of the anti-Lepore variant Hb-Miyada, like the δ chain of Hb-A$_2$ and the $\delta\beta$ chain of Hb-Lepore, is not synthesized appreciably during the reticulocyte stage of red cell maturation Because the δ and the $\delta\beta$ chains have the same amino acid sequence in their N-terminal regions, their mRNAs presumably have the same 5′-nucleotide sequence This, however, is not present in the mRNA coding for the anti-Lepore $\beta\delta$ chain, so that the common pattern of early cessation of synthesis is not determined solely by some feature of the base sequence at the 5′ end of the δ-chain gene

There is evidence for untranslated regions in globin mRNAs Roberts *et al* suggest that these regions may be involved in the stabilization of mRNA, and that they are absent from δ-chain mRNA If this is the case, then the loss of coding for stabilizing regions from the β-chain gene during fusion to form Lepore ($\delta\beta$) and anti-Lepore ($\beta\delta$) genes would account for the relative instability of their respective mRNAs those genotypes that escape capture The concept of genetic feedback regulating population number and bringing about stability in interactions has been extended and championed by Pimintel (*Science*, **159**, 1432, 1968) What happens is that high predator density creates strong selective pressures on the prey This selection alters the genetic complexion of the prey to make it more resistant to attack Such resistance feeds back negatively to limit the feeding pressure of the predator and so stability gradually results Van den Ende's study provides a neat insight into how this process actually works

NUCLEAR PHYSICS

New Giant Resonances

from a Correspondent

It has been known for a long time that a giant electric dipole resonance can be excited in all nuclei by photonuclear experiments of the (γ,p) and (γ,n) type This resonance has an excitation energy of order 70 to 80 $A^{-1/3}$ MeV (where A is the mass number of the nucleus) and a width of a few million electron volts It is visualized as the protons and neutrons oscillating in bulk against one another There have been speculations that other giant resonances with other multipolarities might exist, for example, quadrupole motions in which the nucleon distributions oscillate between prolate and oblate shapes with quadrupole deformations Two types of each might exist, the isoscalar, with isotopic spin quantum number $T=0$, in which the neutrons and protons move together in phase and the isovector ($T=1$) in which they move out of phase The latter type is expected to have a higher vibrational frequency and hence a higher energy In order to qualify as "giants", the excitation strengths of these resonances must exhaust a large fraction of certain sum rule limits

An exciting development recently has been the experimental discovery of a giant isoscalar quadrupole resonance in all the nuclei in which it was looked for (and, in some cases, possibly an isovector one also) One reason the isoscalar one had escaped detection before is that its excitation energy is close to that of the giant dipole (about 2 MeV lower) Furthermore, because its excitation requires electron quadrupole (E2) radiation rather than electron dipole (E1), it is difficult to observe in photonuclear work

The experimental studies of the past few years have been pursued in two parallel and initially independent ways, namely, inelastic electron scattering and inelastic hadron scattering The electron measurements have been made principally at Darmstadt (Buskirk *et al*, *Phys Lett*, **42B**, 194, 1972) and at Tohoku University (Nagao and Torizuka, *Phys Rev Lett*, **30**, 1068, 1973) About twelve nuclei have now been studied, ranging from ^{40}Ca to ^{208}Pb In each case the spectra of inelastic electrons show a peak for excitation of the giant dipole and just below it another peak whose angular distribution is compatible with E2 excitation The strength of the lower resonance exhausts most of the quadrupole sum rule limit Also seen in some cases are indications of another peak at roughly twice the excitation ($\sim$120 $A^{-1/3}$ MeV), also compatible with E2, and it is speculated that this is an isovector resonance

This new resonance was first excited by strong interactions in proton inelastic scattering It was first discovered at Oak Ridge National Laboratory in the spectra of inelastically scattered particles obtained from bombardment of the nuclei by 60 MeV protons, the peak due to excitation of the giant dipole resonance was, of course, also observed (Lewis, Bertrand and Horen, *Phys Rev*, **C8**, 398, 1973) Later it was realized that it had been seen 15 years earlier in the spectra from bombardment by 180 MeV protons[1] At that time the observed peaks had been identified solely with the giant dipole resonance whose position was not known so precisely at that time The excitation strengths observed are in approximate agreement with the corresponding electron measurements Meanwhile the new resonance has also been seen in many nuclei by the inelastic scattering of ^{3}He ions and alpha particles

The angular distributions measured in the electron scattering experiments could not distinguish between E2 and E0 transitions, further the observed strengths were compatible with the sum rule limits for either interpretation (The E0 would be visualized as a breathing mode or radial oscillation in density) These two alternatives would not be decisively distinguished by these early proton measurements although the later measurements favour the E2 choice The ^{3}He and alpha scattering measurements, however, strongly indicate that the resonance has a quadrupole character The theoretical predictions for the cross-sections for monopole excitations which exhaust the sum rule are an order of magnitude smaller than those observed, whereas the predictions for the quadrupole are in agreement with experiment These conclusions have been confirmed by recent studies using polarized protons The consequent left-right asymmetries are predicted to be of opposite signs for E0 and E2 and the measurements are in agreement with E2

The ^{3}He and alpha experiments also provide evidence for the isoscalar nature of the resonance The alpha particle, being isoscalar itself, would only weakly excite an isovector state, whereas the ^{3}He ion suffers no such inhibition The two ions, however, excite the resonance with comparable strengths

Naturally the discovery of this isoscalar quadrupole resonance has aroused new interest in finding other such phenomena The possibility of an isovector quadrupole state at a much higher excitation energy has already been mentioned, and there have been some indications of this from photonuclear experiments also Electron scattering has also shown evidence for giant magnetic dipole excitations at lower energies Preliminary work suggests that there may be fairly strong E3 excitations present as well Of particular theoretical interest (because it relates to the compressibility of nuclear matter) would be the discovery of a giant isoscalar monopole or E0 state A major difficulty that the experimenters have to face is that the spectra from reactions corresponding to these high excitations show large "background" components on which these giant resonances are riding, in most cases they are only giant in the sense that they take up a large part of the corresponding sum rule limits, not that their cross-sections are giant[1]

Clearly the existence or non-existence of such giant resonances must have implications for other nuclear phenomena, and a number of these have been explored Such states may be virtually excited during other processes, only, however, the effective charges needed for the description of electromagnetic transitions between low excited states are mentioned

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POLYPEPTIDES

Corrigendum

from our Molecular Biology Correspondent

In writing about conformation of synthetic polypeptides recently (*Nature*, **244**, 254, 1973), I unaccountably mis-stated utterly one of the results of Rao and Miller (*Biopolymers*, **12**, 835, 1973) This concerns the optical effect of incomplete removal of protecting groups I should have said that this leads to negative ellipticity, where the fully deprotected polymer has a positive Cotton effect, not the other way round Also, in the second paragraph, "dilute salt solutions" should have read "diverse salt solutions" Apologies to those concerned and those confused

RELATIVITY

Signature of a Black Hole

by our Cosmology Correspondent

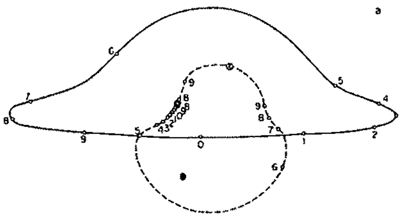
In spite of all the fuss about X-ray stars in binary systems and the difficulty of explaining the presence of these sources by any simple astrophysical model, the case that these systems contain black holes is still not proven Certainly it is true that in some cases, at least, there is good evidence that the underlying object associated with the X-ray emission is both dark, and thus presumably too cool for nuclear burning to be holding it up against gravitational pressure, and also that the object is more massive than the limit above which a cool, non-rotating object will collapse into a singularity without such support But recently two groups have independently pointed out that the compact X-ray sources might be associated with differentially rotating degenerate dwarfs (Brecher and Morrison, *Astrophys J Lett*, **180**, L107 , 1973 , and Lamb and Van Horn, *Astrophys J*, **183**, 959 , 1973)

Lamb and Van Horn, for example, have constructed a detailed, semi-quantitative model of such a star which has a mass of 1 2 to 1 5 $M_{\odot}$ and can explain all the observed properties of Her X-1 It is known that degenerate dwarfs exist, and there seems every reason to believe that they will rotate, perhaps differentially So where is the need to introduce such mathematical curiosities as black holes? Until all simpler explanations of these compact X-ray sources are eliminated, the relativists must look elsewhere for the conclusive proof that these singular predictions of their theories are correct

Two astrophysicists who have done just that are Cunningham and Bardeen They have calculated the detailed effect of a Kerr metric black hole on radiation emitted from a star of 1 $M_{\odot}$ which is in a circular orbit about the hole A combination of Doppler shifts, gravitational redshifts and gravitational focusing combines to modulate the light from the star, as seen by a distant observer , the first two effects determine the surface brightness of the image seen, the third determines its size (*Astrophys J*, **183**, 237 , 1973)

The problem is far from trivial But its solution is worth the effort involved because it suggests a means for detecting black holes which is specific to them No other system could produce a similar light curve, and as an added incentive if such a system were discovered by this signature the detailed variations of brightness and of the image size would provide a test of the strong-field predictions of general relativity

A related investigation of this effect has been carried out by Maeder (*Astron Astrophys*, **26**, 215 , 1973) Both calculations show that the influence of black holes on companion stars should be detectable by present telescopes, and they should lead to an effort by observers to find such peculiarly varying systems



Apparent position of the two brightest images (— , - - -) as functions of time for one particular orbital radius and an observer at a polar angle of 84 24° Numbered intervals define ten equally spaced times

What should the observers look for? The actual light curve seen, of course, depends on the orientation of the orbital plane of the black hole/star system relative to the observer. In addition, the images produced will move around the sky as the star orbits the black hole and its light is bent in different directions And as a third mark of the presence of a black hole in such a system, more than one image is produced (see figure) It might not be possible to resolve the multiple images, which is a pity , but if there is a black hole at the centre of our Galaxy, as some people suggest, then there might well be a good chance of observing this kind of effect Cunningham and Bardeen suggest in particular that the radio signal from a pulsar orbiting a black hole of some 10^6 $M_{\odot}$ at the galactic centre would show the required modulation Extinction along the line of sight to the nucleus makes optical observation impossible, but the pulsar period would be so small compared with the orbital period of the neutron star about the black hole that the radio technique would be quite practicable

Maeder prefers to concentrate on effects which might be produced when a black hole of a few solar masses and a star form a binary system, and he predicts that in some circumstances observers on Earth might see a brightening amounting to several tenths of a magnitude and lasting for several hours In either case, these models and the observable effects they predict provide a much more realistic attack on the problem of the reality or otherwise of black holes than does the approach of invoking such singularities to account for observations which can also be explained by less extreme models

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Acylated·tRNA Metamorphoses

Sprinzel and Cramer, writing in *Nature New Biology* next Wednesday (September 5), suggest that tRNA is aminoacylated exclusively in the 2′-hydroxyl position, but that the aminoacyl group is transferred to the 3′-OH position before the reaction of peptidyl tRNA with aminoacyl tRNA in the ribosome

Evidence for the isomerization of acylated tRNA during protein biosynthesis comes from the study of analogues of tRNA$^{\mathrm{Phe}}$ lacking either the 2′- or 3′-OH group in the 3′-terminal adenosine Only the tRNA$^{\mathrm{Phe}}$-C-C-3′dA can accept phenylalanine, exhibiting the same K_m and only a slightly lower $V_{\max}$ compared with normal tRNA$^{\mathrm{Phe}}$-C-C-A tRNA$^{\mathrm{Phe}}$-C-C-2′dA is, however, a competitive inhibitor of the aminoacylation reaction Such structurally-related molecules as periodate-oxidized tRNA$^{\mathrm{Phe}}$, tRNA$^{\mathrm{Phe}}$-C-C-A$_{\mathrm{oxi}}$ and tRNA$^{\mathrm{Phe}}$-C-C are not competitive inhibitors

Sprinzel and Cramer conclude that, although tRNA$^{\mathrm{Phe}}$-C-C-2′dA can be bound to the active site, aminoacylation can occur only when the hydroxyl group is in the 3′ position

In normal tRNA, acyl migration between 2′ and 3′ OH occurs with a half time of 0 3 s Thus peptidyl tRNA might donate its acyl group to the incoming aminoacyl tRNA by way of only one specific or either by way of both of these two positions on the ribose ring Sprinzel and Cramer's evidence suggests that the ribose 2′-OH group is the sole effective acyl donor

First, they cite earlier evidence that the 2′ analogue of puromycin is inactive as an inhibitor of protein synthesis This suggests that the 3′-peptidyl tRNA isomer is the only acyl donor *in vivo* Their own experimental evidence is consistent with this view because they find that Phe-tRNA-C-C-3′dA cannot be utilized in a poly(U)-directed peptide synthesizing system *in vitro* Free Phe-tRNA$^{\mathrm{Phe}}$-C-C-3′dA on the other hand can undergo hydrolysis (although three times slower than the normal tRNA) Transacylation must therefore be an obligatory step in protein synthesis

This work suggests that there may be highly stringent steric requirements for the ribose isomers for both aminoacylation of tRNA by the twenty or so different synthetase enzymes and for formation of the peptide bond catalysed by peptidyl synthetase in the active site of the ribosome

EARTH'S MAGNETIC FIELD

Seismically Excited?

from our Geomagnetism Correspondent

THE best-known hypothesis for the origin of the geomagnetic field is that the field results from magnetohydrodynamic convective motions in the fluid outer core of the Earth. When this was proposed by Elsasser (*Phys. Rev.*, **69**, 106; 1946) nearly three decades ago, it became the first hypothesis consistent with the observed behaviour of the geomagnetic field at the Earth's surface and is still the most widely accepted view on the origin of the field today. The basic principle of core motion has rarely since been seriously questioned, although Malkus (*Science*, **160**, 259; 1968) alternatively proposed that the fluid circulation in the outer core may be due to the precessional torque on the Earth.

A basic assumption in hypotheses involving motions in the core is that the fluid is at its adiabatic gradient. Two years ago, however, Higgins and Kennedy (*J. geophys. Res.*, **76**, 1870; 1971) concluded that the adiabat for the outer core lies on the "wrong" (solid) side of the melting curve, so that if temperatures were actually distributed along the adiabat the outer core would be solid. They suggested instead that the temperature distribution in the outer core follows the melting point curve. One result of this is that the liquid in the core should be thermally stably stratified and that such stratification may inhibit fluid motion of the kind thought to generate the geomagnetic field. Subsequently, several workers claimed to have resolved this "core paradox" by suggesting that Higgins and Kennedy had miscalculated the adiabatic gradient, that they had wrongly estimated the melting curve of iron, that the outer core may not be pure iron anyway, or that the core comprises a slurry of fine iron particles in liquid suspension. But Kennedy and Higgins (*J. geophys. Res.*, **78**, 900; 1973) later refuted these suggestions, although they did concede that the lower third of the core may have temperatures distributed along an adiabat and thus be capable of sustaining free circulation.

Attempts are still being made to resolve the core paradox; and so for the time being doubt must remain as to whether or not the outer core can be set in motion by convective or precessional forces. In the meantime, however, and notwithstanding the claim by Kennedy and Higgins that their result will "impose severe limitations on any kind of circulation of the fluid in the outer core", Mullan (*Science*, **181**, 553; 1973) has proposed that earthquake waves may be sufficient to produce the motions necessary to the geomagnetic dynamo. According to his calculations, if the total earthquake energy of 10^{26}–10^{27} erg yr^{-1} were transferred to the whole liquid core as kinetic energy and if that kinetic energy were entirely dissipated in one year, the resulting motions would have an energy density of 1–10 erg cm^{-3}. In fact, motions should last about 100 years against viscous damping if the velocity variations have length scales of the order of 500 km or more and assuming the kinematic viscosity to be $\leqslant 10^6$ cm^2 s^{-1}. Thus the kinetic energy available at any time may be derived from more than 100 years of earthquakes, giving energy densities of 10^2–10^3 erg cm^{-3}. Mullan suggests that energy densities in this range may be in equipartition with fields of 50–150 gauss.

Of course, all the energy from earthquakes will not reach the core in practice, although the fraction transmitted from mantle to core should presumably be greater than the 10^{-4} that Won and Kuo (*J. geophys. Res.*, **78**, 805; 1973) calculated would reach the inner core from a large earthquake. But nor need the earthquake energy be transferred to the whole fluid core. Mullan thus concludes that 10^{-4} of the earthquake energy transmitted to the outer 100 km of the outer core would still give an energy density high enough to achieve equipartition with a field of at least 5 gauss at the core-mantle boundary. As more general evidence that earthquakes have global effects, Mullan also points to recent proposals identifying earthquakes as the source of the Chandler wobble. Moreover, correlations of the length of the day with geomagnetic variations and independently with earthquake activity are claimed as indirect evidence for a correlation between geomagnetism and earthquakes.

Finally, Mullan draws attention to two possible implications of a seismic geomagnetic dynamo. The first relates to the obvious geographical correlation between the circum-Pacific seismic belt, where most of the deep earthquakes occur, and the Pacific Ocean, where the non-dipole field and secular variations are anomalously low. Could it be that the seismic excitation of core motions beneath the Pacific, being particularly intense, is sufficient to produce a "semi-permanent center of magnetic action" there with restricted drift?

Second, if the geomagnetic dynamo is excited seismically, the perturbations required to reverse the field may also be seismic. Mullan thus returns to the old idea that field reversals may be induced by the impacts of external bodies on the Earth. For example, 10^{27} erg would be transmitted to the Earth by the impact of a meteorite of mass 10^{15} g arriving at a velocity of 10 km s^{-1}, and if the density of the meteorite were 10 g cm^{-3} its radius would be 3×10^4 cm. Mullan calculates that the average time interval between the impacts of meteorites of such a dimension is 1.7×10^5 yr. This is remarkably close to the characteristic time between field reversals (2×10^5 yr) as deduced by Cox (*J. geophys. Res.*, **75**, 7501; 1970).

ATOMIC MASS

Errors in the Chain

from a Correspondent

A DISCREPANCY with accepted atomic mass values has been observed in a recent measurement of the ^{58}Ni$-^{55}$Co mass difference. In their report to *Physical Review Letters* (**30**, 1255; 1973) Goss, Browne and Rollefson of the University of Notre Dame, Indiana, suggest that there is now reason to doubt all accepted values in this mass region.

Atomic masses are frequently quoted with an uncertainty of less than one part in ten million. For some, this is the result of direct measurements with a mass spectrometer; for most, it follows from an elaborate averaging procedure that takes account of a variety of nuclear reaction data. These data link together the masses of many small groups of isotopes in diverse combinations throughout the periodic table. One isotope may appear in many combinations, so the determination of its mass depends in a complex way upon the masses of its neighbouring nuclei. An error in one mass often implies more widespread problems.

By bombarding ^{58}Ni with 14 and 15 MeV protons and accurately measuring the energy of the outgoing α-particles, Goss *et al.* could relate the mass of the produced ^{55}Co atoms to that of the target atoms. Their result differs by more than three standard deviations from the value calculated from the most recent compilation of atomic masses (Wapstra and Gove, *Nuclear Data Tables*, **9**, 265; 1971). Such a discrepancy might not be particularly alarming were it not for the fact that a difficulty already exists in this mass region. Wapstra and Gove have pointed out that two sets of mass spectrometer measurements on ^{57}Fe disagree significantly with one another, and they warn that there could be a "rather large systematic error" in this whole region. It might well be that the Goss experiment is confirming that fear.

On the other hand, there may be a less traumatic explanation. An examination of the sources used to determine the tabulated ^{55}Co mass value reveals that, while several measurements are included, one has a claimed accuracy that is an order of magnitude better than the others. In effect, it is this value alone that determines the accepted ^{55}Co mass. The method used in that experiment was to measure the total energy released in the beta decay of ^{55}Co, that is the high energy limit of its electron spectrum (see Fischbeck *et al., Phys. Rev.*, **150**, 941; 1966). Achieving high accuracy in such measurements is notoriously difficult. It may well be that there is merely a conflict between two individual experiments rather than a fundamental flaw in the chain of atomic masses.

SOLID STATE PHYSICS

Dense Optical Memory

from a Correspondent

OPTICAL circuits and optical memories may, in the future, play a major part in data transmission, data processing and other electronic equipment (see, for example, *Nature*, **244**, 135; 1973). The various elements necessary for optoelectronic data handling machines are appearing one by one as the research laboratories concerned with computer development compete to make their products faster and smaller. An author from IBM (Wieder, *Appl. Phys. Lett.*, **22**, 487; 1973) now reports further improvements in dense information storage by optical means. Of all the feasible techniques of data storage, optical data storage already has the best potential for high-density use; Wieder's new concept, termed "superresolution", further improves the position of optical storage relative to other forms such as those using magnetic bubbles and semiconductor circuits.

An important method of optical data storage is the local alteration of the order in an amorphous thin film or, alternatively, the local "amorphization" of a crystalline film (see, for example, von Gutfeld and Chaudhari, *J. Appl. Phys.*, **43**, 4688; 1973). The best way of heating the film locally is with a laser beam, and a junction laser is a particularly convenient type to use. Compared with other light sources, a laser can "write" a very small spot on a recording medium. It would, however, be advantageous to work with even small spots, in order to make optical memories even more compact. A junction laser gives a dark spot on a photographic film which is more than 4 μm in diameter, but it would be desirable to reduce that by half so that the grid of spots could have a spacing of, say, 3 μm. The intensity of the laser spot is not uniform from edge to middle, but is, in fact, a gaussian profile, with a width at half maximum of 2.5 μm. The use of a threshold process, such as melting of a thin film, is a way of reducing the size of "spot" recorded. The power level of the beam can be adjusted so that only a small area, of diameter considerably less than the half width of 2.5 μm, is melted. In this way, spots less than 2.0 μm across have been obtained, leading to a correspondingly dense packing of information.

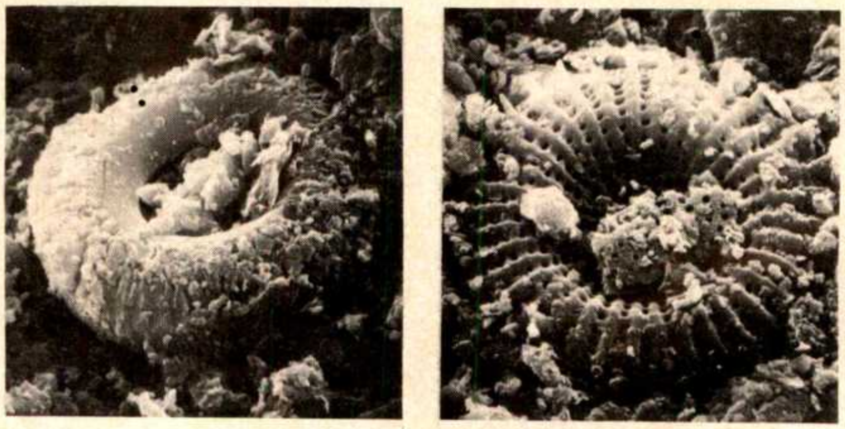
Now, however, comes the problem of reading out this densely packed information. The "read" beam is again gaussian, and will also generate diffraction patterns when interacting with the spot. Thus, if the "read" beam from the laser is again 4 μm in diameter, it cannot separate the information in two adjacent spots that are of 2 μm. Again, a threshold effect has to be found for the reading technique.

Wieder has come up with a very convenient one using the potentiality for threshold effects present in the reading laser itself. The laser is run at a level at which it is luminescing but slightly below the threshold current for lasing. When the beam sweeps over a more reflective area, such as the melted and recrystallized regions representing the "spots" of information, the increased light reflexion provides feedback into the laser resonant cavity and lasing commences. The edge of the spot can thus be detected either by sensing the altered light output of the laser or changes in the current drawn by the laser. The gaussian waveform of the read beam is thus effectively "clipped" by a large and adjustable factor.

In the system described by Wieder, a mixed chalcogenide film was used, containing tellurium, germanium and arsenic, with a preponderance of tellurium. It was evaporated to form a crystalline film, but a film of this composition is easily converted into the amorphous form by melting and rapid cooling. With the laser running continously above threshold, that is without the use of the "clipping" technique, the system could not read dots written on 3 μm centres. But when the laser was run just below threshold, so that the clipping action could operate, the same array of dots was clearly resolved. Extrapolating these trends, by plotting bit separation against modulation depth (essentially the resolving power of the system), it would seem that the threshold method should allow bit separations as low as 2.5 μm, whereas the non-threshold scan should not achieve a separation of less than 5 μm.

The development of the optical memory for computers has clearly come a long way from the form that is so familiar, namely the "IBM card". Bit separation was in the millimetre range for these, whereas it is in the micrometre range for the system now described by Wieder.

Diatomites in Saharan Dust



THE Harmattan is a dust-laden wind which moves south from the Sahara across West Africa during the dry period from December to February. The small dust particles, which mostly range in size from 0.1 to 1 μ, are deposited as the wind meets humid air from Guinea Bay.

The fact that these particles can very effectively penetrate and damage delicate electronic equipment led to a sample being collected from an air filter of a piece of standard ARN-2 equipment at the Ahmadu Bello University at Zaria, Northern Nigeria, and being sent for examination to Dr J. Buczkowski of Warsaw Technical University. Dr Buczkowski found that the dust included very distinct shapes, some of which are typical of warm sea diatomites with dimensions of about 10 μ. Debris particles were less than 1 μ. The figures here show two of the photographs which he obtained with a JSM-U3 scanning electron microscope with a 25 kV electron beam. The magnification was between 3,000 and 10,000.

Other workers have recorded diatomites in the Lake Chad area and Dr Buczkowski considers that study of dust particles originating from the Sahara might provide valuable information on the geological history of the region, as well as help to identify the origin of the Harmattan winds themselves.

Nitrogen Oxides, Nuclear Weapon Testing, Concorde and Stratospheric Ozone

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Although amounts of nitrogen oxides equivalent to the output from many Concordes were released into the atmosphere when nuclear testing was at its peak, the amount of ozone in the atmosphere was not affected.

AT present the ozone layer, which is centred at a height of about 25 km in the stratosphere, is not completely understood At one time it was thought that the oxygen reactions alone, the so-called Chapman classical theory, could account quantitatively for the observed ozone profiles But as knowledge of the relevant rate coefficients and the natural distribution of ozone became more exact, it became apparent that the classical theory gave theoretical ozone profiles with a total ozone content much greater than that observed This discrepancy was for a while accounted for by turning to the so-called "wet chemistry" thesis—that reactions involving water and its dissociation products were responsible for a higher ozone destruction rate than that of the classical theory Again better measurements of the relevant chemical rate coefficients led to the fall of this explanation from favour The current suggestion[1,2] is that naturally occurring nitrogen oxides in the stratosphere, possibly originating from the troposphere and high atmosphere, may play a significant role in the conversion of stratospheric ozone and atomic oxygen to molecular oxygen It would seem[3] that a concentration of 1 to 10 parts per 10^9 of nitric oxide in the stratospheric air is required to produce agreement between measurement and the nitrogen oxide photochemical theory. The actual amounts of nitric oxide in the stratosphere have yet to be established

It is in this context that there has been much speculation recently[3–5] that the oxides of nitrogen produced in the combustors of the jet engines of high flying supersonic aircraft could interact with, and so attenuate, the Earth's ozone shield and increase the ultraviolet radiation reaching the planetary surface It is fair to say that none of these papers contains the necessary full, quantitative consideration[6] of the interaction of radiation, photochemistry and the atmospheric circulation It is, however, incontrovertible that in laboratory conditions NO and NO_2 convert ozone and oxygen atoms to molecular oxygen Such considerations have resulted in the initiation of a number of research programmes in the United States, Britain and France to study the climatic consequences of the operation of fleets of supersonic aircraft

Any process which heats air above $\sim$2,300 K will produce significant quantities of NO as an equilibrium constituent Examples of such heating include the shock waves from nuclear explosions as well as the operation of the combustion chambers of aircraft jet engines The actual amount of nitrogen oxides remaining at ambient temperatures will depend on the rate at which the heated air cools through the 2,500 K temperature region It may be that massive amounts of nitrogen oxides have already been injected into the stratosphere during the various nuclear testing programmes

Shock Wave

In order to calculate the amounts of nitrogen oxides produced in the shock waves of nuclear explosions, it is necessary to know the pressure-temperature history of each parcel of air through which the shock front passed We used the mathematical description of the spherical shock wave given by Taylor[7] to calculate the pressure-temperature histories of seven spherical surfaces enclosing fixed masses of air around the explosion centre We then obtained values of pressure and temperature of each spherical shell enclosed by these seven surfaces by averaging the values at the two boundaries The innermost shell (1), which includes the explosion centre, was taken to have the temperature and pressure history of the first spherical boundary This was carried out for explosions of 1, 10 and 60 Mton TNT equivalent The results of these calculations are given in Fig 1

Zel'dovich and Raizer[8] point out that the theory is not strictly applicable to the central regions of the explosion (shells (1) and (2)) where radiative effects probably dominate Also the theory becomes more approximate when the pressure in the shock front is less than about ten times that of ambient

In arriving at the curves in Fig 1, a constant value, 1 4, of the ratio of specific heats γ has been assumed Although at higher temperatures, γ is reduced from its ordinary tropospheric value of 1 4 by the absorption of energy in the form of molecular vibrational quanta, at very high temperatures increasing dissociation may be expected to compensate for this effect Taylor noted that his calculations fitted the observed behaviour of the fireball in the first nuclear test in New Mexico better for γ=1 4 than for γ=1 3 The shock wave has been assumed to propagate spherically in a uniform atmosphere at 290 K and 1,000 mbar For the largest explosion considered (60 Mton), the radius of the 2,000 K surface is about 3 km, at which height this approximation is acceptable as demonstrated by Korobeinikov's more accurate description[9] of shock wave propagation in a real atmosphere

Chemical Kinetics of Heated Air

The production of NO in shock-heated air has been directly measured in laboratory shock tube experiments at temperatures between 2,300 K and 6,000 K by Camac and Feinberg[10]

Mole fractions of nitric oxide, [NO]/[M], of up to 0.1 were observed, the experiments applied, however, to short reaction times (several microseconds) and pressures from 0.01 to 0.07 atm. This is in contrast to the conditions following a weapon burst, where, after a few hundred milliseconds, pressure relaxation rates are of the order of 50 atm s^{-1} and cooling rates are of the order of 2,000 K s^{-1}. The masses of the concentric shells of air heated above 2,000 K are typically of the order of 10^{12} g. In these circumstances the best *a priori* way to calculate production of nitrogen oxides would be to start with a chemical kinetic mechanism composed of the elementary processes thought to be relevant and derive the set of simultaneous differential equations describing the variation in time of the number densities of the molecular species involved. These equations should then be solved, by numerical integration, for a particular air mass, through its pressure-temperature history as a function of time down to times and temperatures where the NO production and destruction rates are slow compared to the cooling rate.

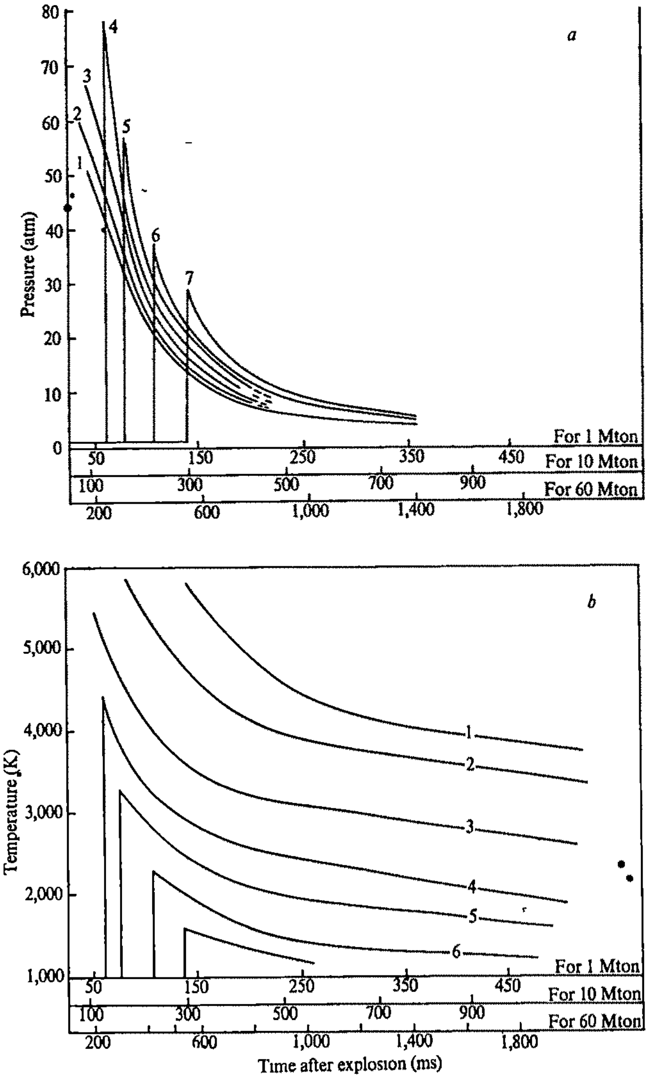


Fig 1 Pressure (*a*) and temperature (*b*) histories for seven shells due to the shock wave around 1, 10 and 60 Mton explosions. Masses in units of 10^{12} g per shell are

Shell No	1 Mton	10 Mton	60 Mton
1	0.115	1.15	6.9
2	0.115	1.15	6.9
3	0.103	1.03	6.2
4	0.075	0.75	4.5
5	0.145	1.45	8.7
6	0.273	2.73	16.4
7	0.283	2.83	17.0

The elementary chemical processes used in calculating the nitrogen oxide production in the hot air masses created by the nuclear shock wave are as follows

$$N_2+M \rightarrow N+N+M \quad (1)$$
$$N+N+M \rightarrow N_2+M \quad (2)$$
$$O_2+M \rightarrow O+O+M \quad (3)$$
$$O+O+M \rightarrow O_2+M \quad (4)$$
$$NO+M \rightarrow N+O+M \quad (5)$$
$$N+O+M \rightarrow NO+M \quad (6)$$
$$NO_2+M \rightarrow NO+O+M \quad (7)$$
$$NO+O+M \rightarrow NO_2+M \quad (8)$$
$$N_2O+M \rightarrow N_2+O+M \quad (9)$$
$$O_3+M \rightarrow O_2+O+M \quad (10)$$
$$O+O_2+M \rightarrow O_3+M \quad (11)$$
$$O+N_2 \rightarrow N+NO \quad (12)$$
$$N+NO \rightarrow N_2+O \quad (13)$$
$$N+O_2 \rightarrow O+NO \quad (14)$$
$$O+NO \rightarrow N+O_2 \quad (15)$$
$$O+NO_2 \rightarrow NO+O_2 \quad (16)$$
$$NO+O_2 \rightarrow O+NO_2 \quad (17)$$
$$N+NO_2 \rightarrow NO+NO \quad (18)$$
$$NO+NO \rightarrow N_2O+O \quad (19)$$
$$O+N_2O \rightarrow NO+NO \quad (20)$$
$$N+NO_2 \rightarrow N_2O+O \quad (21)$$
$$NO+NO+O_2 \rightarrow NO_2+NO_2 \quad (22)$$
$$NO_2+NO_2 \rightarrow NO+NO+O_2 \quad (23)$$
$$O+O_3 \rightarrow O_2+O_2 \quad (24)$$
$$NO+O_3 \rightarrow NO_2+O_2 \quad (25)$$

Excited species of both atoms and molecules have not been included, though some, for example $O(^1D)$, $O(^1S)$, $O_2(^1\Delta)$, $O_2(^1\Sigma_g^+)$, $N^2(D)$, $N_2(A^3\Sigma_u^+)$, $N_2(B^3\Pi_u)$, $NO(A^4\Pi)$ and $NO(A\Sigma^2)$, may be expected to be populated or chemically produced at the higher temperatures. Justification for this omission is that the pressures which accompany the high temperature ensure that collisional deactivation of excited species is likely to be efficient. Also possible coupling between molecular motions, chemical processes and the kinetic energy of the shock wave in the air immediately behind the shock front has been considered to be negligible because a comparison of the time taken for the shock to traverse the thickness of the shock front (a few mean free paths) and the time scale of the chemistry indicates that absorption of energy from the shock by chemical processes has but a small effect upon the shock front velocity in those regions where radiation effects are unimportant.

The integrations were carried out using rate coefficients taken from recent authoritative reviews as summarized in Table 1. With the exception of reactions (3) and (4), the rate coefficients have been adjusted for molecular nitrogen as the third body M. For reactions (3) and (4), the larger third-body efficiencies of atomic and molecular oxygen were used. Where the reverse process of a reaction occurred, values were chosen to be compatible with the thermochemical equilibrium constant.

The integrations were carried out by a semi-implicit scheme, programmed in ASSEMBLER, a low level IBM language. Initially, a simple Euler first-order forward time step method was used to perform the integration. A prohibitively small time step of 10^{-10} s was required by this method. By setting nitrogen atoms and ozone to equilibrium, this was lowered to 5 × 10^{-7} s for shell (6), with its temperature of 2,300 K. The semi-implicit method could run satisfactorily, without setting any species to equilibrium, using a timestep of 10^{-6} s at 2,300 K,

5×10^{-7} s between 2,300 K and 3,300 K (shell (5)), and 10^{-7} s between 3,300 K and 4,400 K (shell (4)). The results obtained by the different methods at 2,300 K agreed closely, to have run the forward time step method at higher temperatures would have involved setting nitric oxide itself to equilibrium, thus defeating the purpose of the exercise The semi-implicit scheme used the relation

$$Y_{n+1}(i)=\frac{Y_n(i)+P(i)\Delta t}{1+Q(i)\Delta t}$$

where $Y_{n+1}(i)$ is the concentration of the ith constituent at the $(n+1)$th time step and $P(i)$ and $Q(i)$, functions of rate coefficients and concentrations of other species, are defined by the general chemical kinetic differential equation

$$\mathrm{d}Y(i)/\mathrm{d}t=P(i)-Q(i)\ Y(i)^m$$

where in this case $m=1$ or 2 At every time step each species was advanced in turn by this method, while the remainder were held constant. This method does not simultaneously solve all the continuity equations, and so cannot be guaranteed to conserve chemical identity (that is to say the total numbers of oxygen and nitrogen atoms). Chemical conservation was in fact obeyed quite well except in the few integrations which went to numbers of time steps greater than about 2×10^6 In all cases, however, results are quoted from integrations where conservation of N atoms and of O atoms was ensured by scaling after each time step to the density implied by the pressure and temperature history derived from Taylor's equations Results of typical integrations are shown in Fig 2 The rate coefficients were recalculated at descending 50 K intervals, after assuming a step perturbation of air from STP to the initial pressure and temperature values on each of the curves (4), (5) and (6) of Fig 1. The air in the outer shell (7) (curve (7)) never reaches a high enough temperature to produce significant amounts of NO.

Table 1 Rate Coefficients

Reaction	A	N	E	Reference
1	3.73×10^{21}	-1.6	224,900	11
2	2.25×10^{21}	-1.6	0	11
3	4.79×10^{18}	-1.0	118,700	13
4	2.38×10^{17}	-1.0	340	13
5	2.27×10^{17}	-0.5	148,830	14
6	6.45×10^{16}	-0.5	0	14, 12
7	1.54×10^{16}	0	65,000	14
8	1.47×10^{15}	0	$-1,870$	14
9	1.30×10^{15}	0	58,000	15
10	3.89×10^{14}	0	22,720	13
11	6.46×10^{12}	0	$-2,100$	13
12	1.36×10^{14}	0	75,400	14
13	3.10×10^{13}	0	334	14
14	6.43×10^{9}	$+1.0$	6,250	14
15	1.55×10^{9}	$+1.0$	38,640	14
16	1.00×10^{13}	0	600	14
17	1.00×10^{12}	0	45,500	14
18	3.60×10^{12}	0	0	14, 16
19	9.40×10^{11}	0	66,000	14
20	2.50×10^{13}	0	26,900	14
21	1.20×10^{12}	0	0	14, 16
22	2.43×10^{9}	0	$-1,046$	14
23	4.00×10^{12}	0	26,900	14
24	1.20×10^{13}	0	4,790	13
25	5.72×10^{11}	0	2,460	34

$k=AT^N\exp(-E/1.987T)$

k is in $(\mathrm{cm^3\ mol^{-1}})^n\ \mathrm{s^{-1}}$ units, E is in calorie $\mathrm{mol^{-1}}$ ($n=1$ for a two-body process and $n=2$ for a three-body process)

The results of these calculations are given in Table 2 in which the nitric oxide yield for each concentric shell is listed, together with the total air mass in that shell for explosions of 1, 10 and 60 Mton equivalent TNT It is seen that the NO yields for 1, 10 and 60 Mton explosions are 0.49, 5.4 and 35.5×10^{10} g respectively The yield in the range 1 to 10 Mton is about linear, with 5×10^9 g of NO being

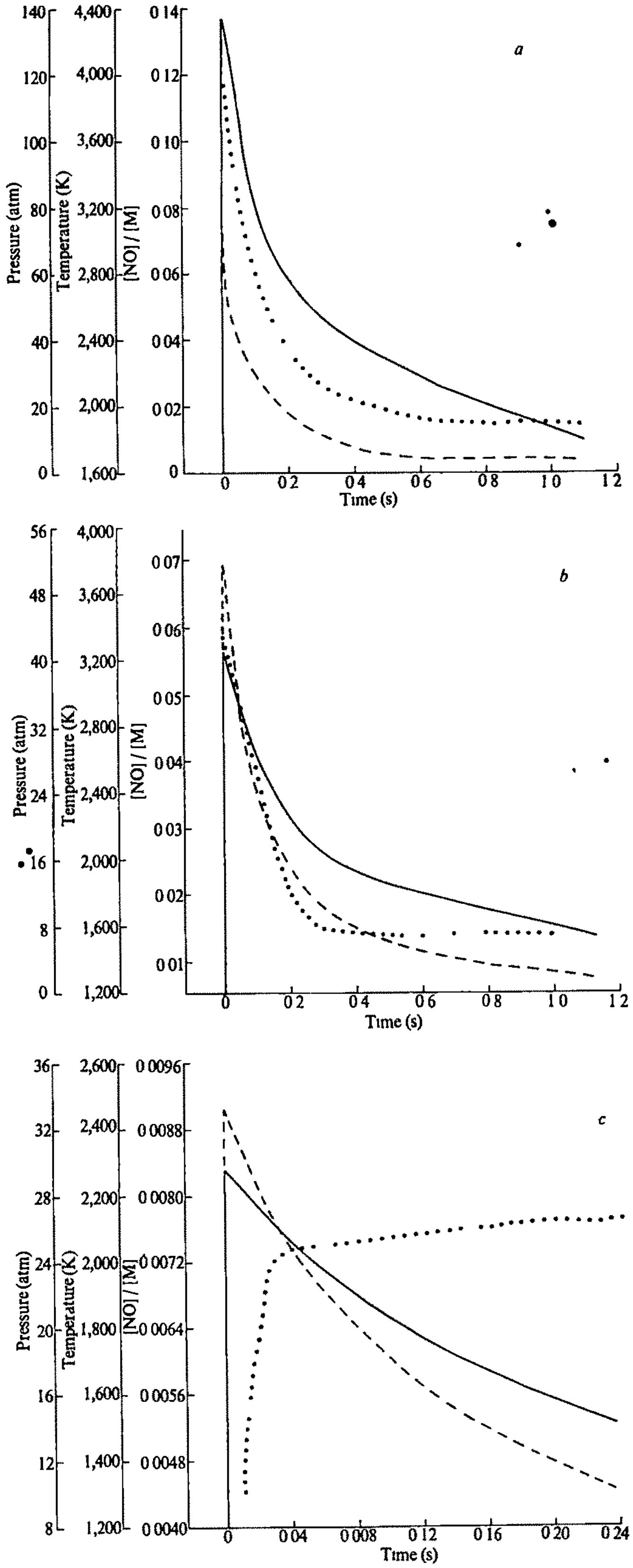


Fig. 2 Nitric oxide concentrations as a function of time for a 10 Mton explosion *a*, Shell (4), shock starts 155 ms after ignition, *b*, shell (5), shock starts 197 ms after ignition, *c*, shell (6), shock starts 273 ms after ignition The pressure and temperature histories are also plotted ——, Temperature, - - -, pressure, ⋯, [NO]/[M]

produced per Mton of explosive energy. This linearity breaks down somewhat for the 60 Mton explosion because in the outermost of the shells producing significant amounts of NO (shell (6)), the NO production is slow enough to be dependent on the time spent at high temperatures, rather than the cooling rate as is the case for the inner shells. Sixty megatons is about the size of the largest individual nuclear explosion ever made, in Russia in 1962.

The deduced production of 5×10^9 g per Mton of explosive power can be compared with the findings of three previous studies.

The first by Davies[17] was primarily concerned with the chemical composition of the air in the shock wave and how the resulting changes in γ would affect the shock propagation. He did, however, conclude on the basis of a statistical mechanical treatment of equilibrium constants that at 4,000 K 4.6% of nitric oxide would be present. He also concluded that no NO would be produced at temperatures of 3,000 K or lower, that is because the statistical mechanical approach does not allow for the changes in the chemical reaction rates with temperature being slower than the rate of change of temperature. The amount of NO left after the passage of the shock wave was not of concern in this study.

Table 2 Calculated NO Production

Explosion strength (Mton)	Shell No	Air mass in shell (10^{12} g)	[NO]/[M]	[NO] (10^{10} g)	[NO] (10^{32} molecules)
1	4	0.075	0.017	0.13	0.26
	5	0.145	0.016	0.23	0.46
	6	0.270	0.005	0.13	0.26
			Total	0.49	0.98
10	4	0.75	0.015	1.2	2.4
	5	1.45	0.014	2.1	4.2
	6	2.70	0.008	2.1	4.2
			Total	5.4	10.8
60	4	4.5	0.015	6.8	13.6
	5	8.7	0.013	11.1	22.2
	6	16.4	0.011	17.6	35.2
			Total	35.5	71.0

In the second, Zel'dovich and Raizer[18] assume that all the air that had been taken to temperatures greater than 2,300 K in the shock wave would ultimately have equilibrium NO concentrations frozen at values characteristic of 2,300 K when returned to ambient temperatures. On this basis they concluded that a 20 kton equivalent TNT explosion would yield a concentration of NO of about 1%, equivalent to about 50 ton. On a linear extrapolation this means that a 1 Mton explosion would yield 2.5×10^9 g. This is about half the yield indicated by the more comprehensive calculations outlined here. In the third study, Foley and Ruderman[19], simply took one-third of the liberated explosive energy yield as remaining as thermal energy in the buoyant hot air and assumed that this energy would be used in heating a mass of air to 2,000 K. The physical basis of this assumption is not readily apparent from detailed studies of Taylor[7] and Brode[20]. They further assumed that all this air instantaneously produced a concentration of 0.8% NO. The time scale for NO production for curve (6) of Fig. 2 of this article demonstrates one limitation of this approach. However, this simplified treatment of the physics and chemistry of nuclear explosions yielded a similar result (10^{10} g of NO per Mton explosive energy), higher than that of our method by a factor of two.

What are the limitations of the treatment presented here? In arriving at the nitric oxide production rate, the inner three shells, denoted in Fig. 1, and containing 0.33, 3.3 and 20×10^{12} g, respectively, for 1, 10 and 60 Mton events, have not been included. This is not only because of the inapplicability of the Taylor formulations to these inner regions where radiative transfer may be relatively important but it might also be argued that these high temperatures gases absorb the ionizing radiations from the innermost region, so shielding the nitric oxide in the outer shells (4), (5) and (6). The chemistry of a hot ionized air mass, subjected to radioactive emissions, is not easily modelled. Any nitric oxide production in these innermost shells will be additional to 5×10^9 g per Mton deduced from the outer shells. Also, all the calculations apply to a spherical shock wave. For explosions on or near the ground some of the energy would be absorbed in the Earth rather than propagated in the atmosphere, leading to a somewhat smaller nitric oxide production.

As mentioned earlier, a value of 1.4 for γ, the ratio of specific heats, was used in calculating the pressure-temperature histories of the shock wave. To test the effect of decreasing γ, the pressure-temperature histories were recalculated for a 10 Mton event using $\gamma = 1.3$. The nitric oxide production was now attributed to shells (3), (4) and (5) rather than (4), (5) and (6). It was found that the total nitric oxide production was decreased to 4.5×10^9 g per Mton.

The overall calculated NO production for an explosion was found not to be very sensitive to variation to any one of the rate coefficients k_3, k_4, k_{12}, k_{13}, k_{14}, k_{14}, k_{19} and k_{20} within their experimental limits. But simultaneously setting the first six of these (k_3 to k_{15}) to their lower limits and the other two (k_{19} and k_{20}) to their upper limits reduced total nitric oxide production to 2.7×10^9 g per Mton. Inspection of the course of the integrations showed that reactions (3), (12) and (14) were the chief producers of nitric oxide and reaction (19) was the principal destroyer. This is in agreement with the experimental observations of Camac and Feinberg. Thus the value of 2.7×10^9 g per Mton is a lower limit in the light of current knowledge of rate coefficients.

The amounts of NO_2 and O_3 generated by explosions also formed part of the solutions of the differential equations. It was found that NO_2 was always less than 1% of the nitric oxide production and that the O_3 production was negligible. The fact that the NO_2 amounts were so small provides some justification for omitting the higher oxides of nitrogen (NO_3, N_2O_5). In these calculations, the temperature history below 1,500 K was not considered. Needless to say there will be considerable conversion of NO to NO_2 as the air mass cools to ambient. This would account for the observations[22] of an orange colour to the nuclear cloud at high altitudes.

The chemical model outlined here is strictly speaking applicable only to dry air. In the real atmosphere, it is possible that a number of reactions involving water and its dissociation products should be incorporated. It is difficult to visualize a chemical mechanism at the relevant elevated temperatures by which water or its dissociation products at atmospheric mixing ratios could prevent the formation of NO. Species such as HNO, HNO_2, HNO_3 have dissociation energies less than NO_2, thus in the absence of some catalytic destruction of NO or NO_2 by H, OH, HO_2 and H_2O processes such as

$$OH + NO + M \rightarrow HNO_2 - M$$

cannot prevent the formation of NO in the shocked air masses. Further calculations on this point are in progress, but it is a fact that in the emissions of jet engines the gases contain high amounts of water and dissociation products and this does not apparently inhibit production of NO.

Nitrogen Oxide Production by Concorde

The recommended value[21] for the emission of nitrogen oxides from the Concorde's Olympus Mark 602 engines is 13.8 g of NO per kg of fuel consumed, which is rather larger than estimates based on measurements made at the National Gas Turbine Establishment, Pyestock. At a cruise altitude of about 55,000 foot, the engine's fuel consumption is about 4,550 kg h^{-1} per engine. Thus assuming a trans-Atlantic crossing requires $2\frac{5}{8}$ h flying time in the stratosphere, the total nitrogen oxide production per flight expressed in terms of NO is 670 kg. Thus one Concorde crossing the Atlantic, four times a day each day of the year produces 9.8×10^5 kg yr^{-1} of NO.

Table 3 gives a year by year summation of all nuclear explosions[19,22–24] greater than 20 kton TNT together with the associated NO production deduced from the calculated yield of 5×10^9 g per Mton. In the fourth column is the number of Concordes that would have to fly across the Atlantic four times a day each day of the year to produce the same amount of NO as that year's nuclear weapon testing.

It is seen that the nuclear testing is equivalent during the period 1952 to 1958 to more than 100 fully operational Concordes. During 1961 and 1962, as many as 800 Concordes would have had to have been fully operational throughout the two years for the same gross NO injection. The assumption is made that all nitrogen oxides produced in explosions are ultimately transported into the stratosphere. As the greater proportion of radioactive débris in an air burst of 1 Mton or greater is injected into the stratosphere[25], it is not unreasonable to assume that all nitrogen oxides will reach the stratosphere in a similar manner. Although Table 3 gives a summation of nuclear explosions greater than 20 kton TNT, the total yield of explosions between 20 kton, which probably do not inject material into the stratosphere[25], and 1 Mton, which probably do, is only a small proportion of the total. The inclusion of these low yield explosions will make no significant differences to the estimates of the stratospheric injection of nitrogen oxides.

Table 3 Calculated Annual NO Production from all Nuclear Tests greater than 20 kton and the Equivalent Number of Fully Operational Concordes

Year	Mton TNT	NO production 10^7 kg	Equivalent No of fully operational Concordes
1952	11.1	5.5	54
1953	0	0	0
1954	48.5	24.2	237
1955	2.0	1.0	10
1956	26.0	13.0	127
1957	13.5	6.7	66
1958	61.9	30.9	303
1959	0	0	0
1960	0	0	0
1961	120.6	60.3	591
1962	213.5	106.7	1,047
1963	0	0	0
1964	0	0	0
1965	0	0	0
1966	1.4	0.7	7
1967	3.5	1.7	17
1968	7.6	3.8	37
1969	3.0	1.5	15
1970	6.1	3.0	30
1971	1.6	0.8	8
1972	0	0	0

There will, however, be obvious differences between the stratospheric distribution due to aircraft emissions and that due to more rapid injections by explosions. In the first place, the aircraft injections are confined to the limited region of air routes, and operational flight altitudes in the lower stratosphere. The nuclear injections cover a much wider altitude range, depending on the strength of the explosion, the cloud of débris from a 1 Mton event typically stabilizes[25] at a height of about 22 km whereas that of a 10 Mton event would reach about 32 km. Thus the Concorde emissions at the operational height of 17 km are always below the maximum in the vertical ozone profile, while the nitrogen oxides from nuclear explosions could well stabilize in the same height range as the ozone maximum.

It must therefore be accepted that amounts of NO at least comparable with those expected from large fleets of Concorde aircraft have already been directly injected into the stratosphere. If the atmospheric ozone budget is sensitive to injections of anthropogenic nitrogen oxides then one would expect the effects of the nuclear testing programme to be reflected in the past records of total ozone amounts. This applies especially to 1961 and 1962.

Ozone Records

The total amount of ozone in the atmosphere above any point on the Earth's surface is highly variable, with large fluctuations from day to day and with a well established annual cycle which has a maximum in the early spring and a minimum in the late autumn. If the nitrogen oxides from the testing of nuclear weapons have affected total amounts of ozone, then one would expect this to be reflected in the ozone records since 1952, with special emphasis on the years 1961 and 1962 when weapons yielding 334 Mton were exploded, more than half the total explosive energy of all tests. Those tests before 1952 were all of less than 1 Mton yield and contributed little to the total stratospheric injections.

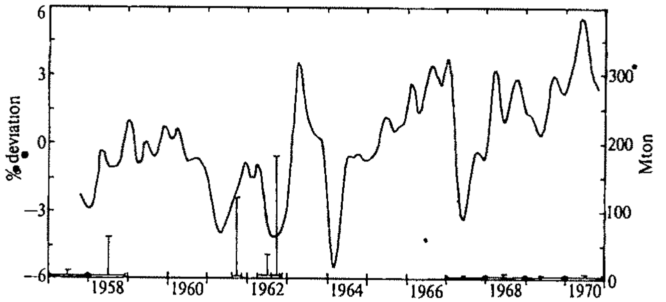


Fig 3 Smoothed deviations from monthly means of total ozone from seventeen stations in the period 1957 to 1970 and the intensity and timetable of nuclear explosions in this period. ——, Deviation, ⊥, nuclear events.

In Fig 3 are plotted ozone data from the seventeen stations in the northern hemisphere with the longest continuous record (see Table 4). The deviation from the monthly mean, expressed as percentage of that mean, is plotted monthly as a function of time. In this way the annual and short term fluctuations are removed. Also the mean of the seventeen stations was subjected to conventional five term binomial smoothing.

The stations were selected on the following criteria. The records exist from 1957 or 1958, the beginning of the IGY period, when many more stations commenced operation, they do not have gaps of more than 18 consecutive months in their data, and they have more than 110 monthly mean values for the total period 1957 to 1970. Stations making measurements with the Russian filter ozonometer were excluded because it has been demonstrated[26] that results from these instruments differ significantly from those of the Dobson ozone spectrophotometer for solar zenith angles greater than 60° or in the presence of haze. This may be important on account of secular changes in haze (R N Kulkarni, private communication) Furthermore only ozone measurements in the northern hemisphere are considered because most nuclear weapon débris has been injected there In any case very few stations in the southern hemisphere would have met the criteria of long term continuity The periods of weapon testing together with total megaton yield for each of nine periods are also indicated on Fig 3 The American equatorial and Russian high latitude tests of 1961–62, are separated on Fig 3, with the American tests coming between the two periods of Russian tests

It might be expected that if nitrogen oxides from the nuclear explosions are to modify the total ozone amount, then this would be reflected in the records, covering the northern hemisphere, delayed by a period dependent on stratospheric mixing times and relevant chemical reaction rates It seems to us that these records do not provide evidence for such a modification

Table 4 Ozone Records of the Stations Used in Fig 3

Station	No of months	Mean total ozone	Slope (% per decade)	Error of slope (σ)
Arosa (47° N 10° E)	158	334	1 2	0 9
Cagliari Elmas (39° N 9° E)	161	329	8 6	0 9
Camborne (50° N 5° W)	115	338	6 3	1 7
Edmonton (54° N 114° W)	162	357	2 9	1 0
Kagoshima (32° N 131° E)	151	289	1 9	1 2
Kodaikanal (10° W 77° E)	161	255	10 6	0 5
Lerwick (60° N 1° W)	151	348	7 2	1 2
Messina (38° N 16° E)	141	346	3 5	0 9
Napoli (41° N 14° E)	137	301	−1 3	1 1
New Delhi (29° N 77° E)	159	270	7.8	1 1
Oxford (52° N 1° W)	162	353	4 3	1 0
Resolute (75° N 95° W)	143	390	3 6	1 8
Reykjavik (64° N 22° W)	134	339	−1 7	1 9
Sapporo (43° N 141° E)	155	371	1 0	0 8
Tateno (36° N 140° E)	160	325	0 0	0 9
Tromsø (70° N 19° E)	121	331	0 6	2 0
Vigna Di Valle (42° N 12° E)	162	341	1 1	0 9
Mean of stations	162	330	6 3	1 7

It has, however, been suggested by Johnston *et al*[27] on the basis of an analysis of the records of ozone measuring stations from 1960, including those in the Soviet Union and some in the southern hemisphere, that in the northern hemisphere there was a significant decrease (−7 6% per decade) in ozone during 1960–62, followed by an increase (+5 6% per decade) in 1963–70 Johnston *et al* argue on the basis of these figures, that "the oxides of nitrogen from nuclear bomb tests of 1952–62 constituted a measurable injection and the consequent reductions of ozone may be ascribable (perhaps only in part) to this injection experiment" They also speculate that the ozone increase in 1963–70 may represent a recovery from the effects of the test period

The ozone data going back to late 1957 given in Fig 3, do not support the contention that the period 1960–62 is of any particular significance with respect to the periods of nuclear testing Moreover there is considerable danger in comparing ozone trends over an interval of 3 yr This is demonstrated in Fig 4 in which the 3 yr slopes of the seventeen station ozone records are plotted monthly It is seen that the slopes vary between about +26% and −13% per decade and so there is no significance to the −7 6% per decade obtained by Johnston for 1960–62 Indeed during 1963–70, there was a period when the 3 yr slope was also negative

The upwards tendency of the trace of Fig 3 since 1961 agrees with the findings of Komhyr *et al*[28] that there has been an increase of total ozone of up to 10% at a number of stations during the past decade (1961–70)

There have been a number of other studies of trends of ozone based on much longer records of data Notably Willett[29] and Christie[30], both on the basis of records going back to 1933, detected a negative and largely unexplained correlation of total ozone with sunspot number The ozone minimum precedes the sunspot maximum by about 20 months London and Oltmans[31] were, however, unable to find such a correlation in the Arosa and Tromso records, which formed the bulk of the Willett, Christie data before 1945 Paetzold *et al*[32], on the evidence of direct balloon-borne optical ozone soundings over central Europe between the years 1951 to 1972, report a positive correlation between sunspot number and the ozone amounts between 20 and 30 km The evidence for this correlation is, however, not conclusive because of the lack of data in the first half of the period

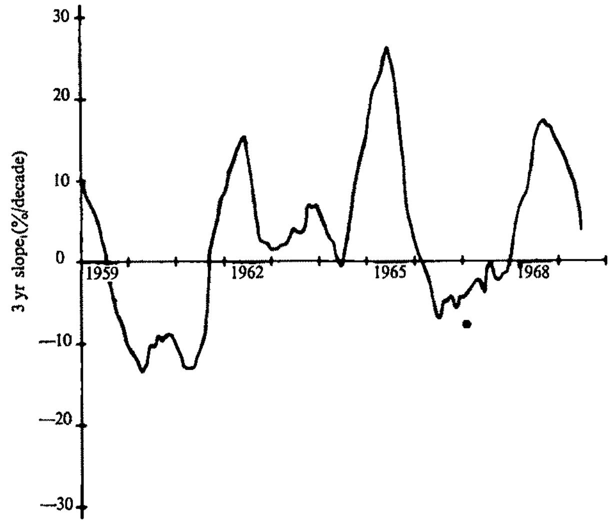


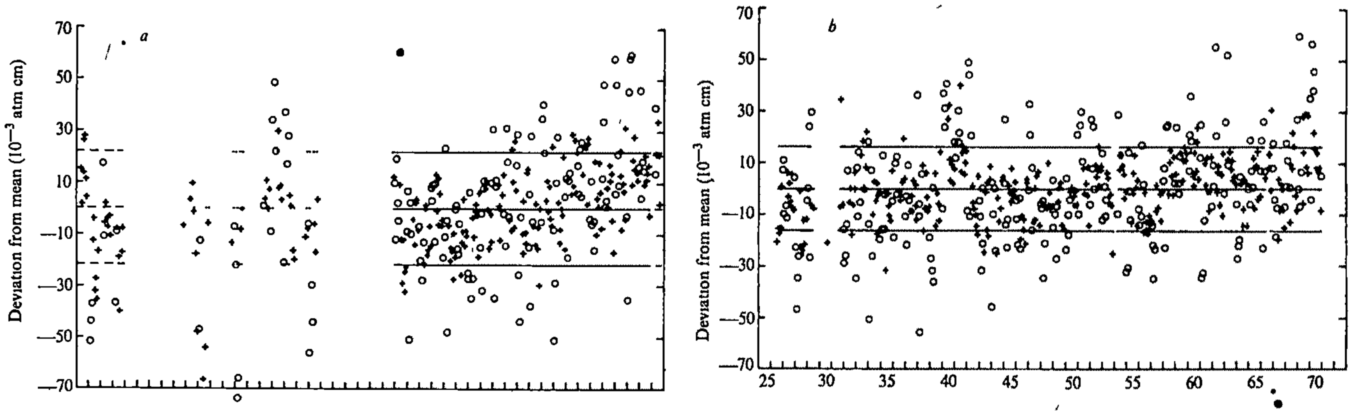
Fig. 4 Percentage increase expressed in % per decade for the total ozone calculated from the deviations of the monthly means for seventeen stations over 3 yr intervals from 1959 to 1969

There are only two ozone observing stations with reasonably complete long term records These are Arosa and to a lesser degree Oxford, both from 1926 In Fig 5 the deviation from the monthly mean is shown for both these stations The Oxford data between 1933 and 1944 have not previously been published, those for Arosa are given by Perl and Dutsch[33]

These long term records demonstrate the high variability in total ozone over a wide variety of time scales and indicate the difficulty in detecting any short term trends In common with other data presented here, there is nothing to suggest that nitrogen oxides from the testing of nuclear weapons in the atmosphere have had any effect on the total ozone

Implications

In this article the production of nitrogen oxides in the shock wave of explosions associated with the testing of nuclear weapons in the atmosphere has been calculated This has allowed the total injection of nitrogen oxides into the stratosphere to be deduced for each year in which nuclear tests have taken place These amounts have been compared with those expected from the engine exhaust products of fleets of Concordes each flying in the stratosphere for more than 10 h every day of the year We conclude that past nuclear explosions have been equivalent, as far as nitrogen oxide stratospheric injections are concerned, to large numbers of these fully operational Con-



N yr mean and standard error

	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Mean
Oxford													
Mean	348	384	391	395	388	371	350	336	308	294	291	310	348
s e	29	33	29	26	18	14	19	13	23	19	19	17	22
N	26	24	30	31	28	31	33	26	32	33	23	25	342
Arosa													
Mean	336	361	370	371	361	340	322	308	289	280	283	307	327
s e	21	26	24	19	14	12	10	11	12	11	12	15	16
N	41	41	42	42	42	40	41	44	43	41	43	42	502

Fig. 5 Deviation of monthly total ozone from the mean of that month for Oxford, 52° N 1° W (*a*), and Arosa, 47° N 10° E (*b*), from 1925 to 1971 ○, Values for January to March inclusive, when the total ozone is at its most variable, +, values for all other months The units represent the equivalent thickness of ozone at standard temperature and pressure

cordes For instance, during the years of maximum nuclear activity, 1961 and 1962, the number of Concordes giving equivalent nitrogen oxide emissions would have been about 600 and 1,000 respectively Analysis of the ozone records reveal no detectable changes in the total atmospheric ozone during and after the periods of nuclear weapon testing Although the two modes of nitrogen oxide injection may not be identical from the meteorological view point, the conclusion that massive injections of nitrogen oxides into the stratosphere do not upset the ozone layer seems inescapable Such a conclusion has profound implications for our understanding of the photochemical processes in the stratosphere, as it is only by postulating an ozone sink due to natural nitrogen oxide at the level of 1 to 10 parts per 10^9 that current theories are able to account for the natural concentrations of ozone in the stratosphere It may be that other factors such as solar radiation, stratospheric circulation, refinement of chemical rate coefficients and hitherto unconsidered chemical sinks may all play a part in bringing theory closer to measurement

We thank Professor G M B Dobson for making available the unpublished Oxford ozone records and R Smart for help with analysis of the records

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Dynamic Mixing of Water and Lava

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The heat content of lava is such that if roughly equal volumes of lava and water are rapidly mixed, the resulting pressure may be enough to cause further dynamic mixing of a lava flow under the ocean leading to a catastrophic explosion. The same mechanism of self-sustained mixing may explain several foundry explosions of liquid metal and water, and others of large volumes of liquid natural gas and water where the water serves as the hot fluid. The Krakatao volcanic explosion, equivalent to 200 megatons, may have the same explanation.

During the Heimaey eruption it was suggested that an underwater lava flow threatening to close off the island's harbour might be dealt with by high explosive The idea was that the resulting rapid mixing with water would thicken the lava and impede the flow We planned such an explosion with the help of the Icelandic government, the Icelandic Coast Guard and the US Navy, but the day before the detonation we realized the awesome possibility that once mixing was initiated it might be self sustaining in that the high pressure steam produced might cause further mixing until all the lava had exchanged its heat with the water above it The energy released might have come to between 2 and 4 megatons Naturally the experiment was called off

Since then we have found several references[1-3] to unexplained, but sometimes disastrous industrial explosions when molten aluminium, iron, or salt, came suddenly in contact with water In no case was the release of chemical energy significant In general, no detailed explanation is offered other than that the liquids must break up into small particles for rapid heat transfer[4] In some cases, such as explosions of liquid natural gas (LNG) and water (when the water is the hot fluid and the LNG is the vaporizable liquid), it has been suggested[5,6] that delayed nucleation boiling may be involved

We believe that all cases of contact between a hot fluid and a cold vaporizable fluid are potentially explosive by a process of dynamic self-sustained mixing The amount of liquid necessary is associated with the Reynolds number of the mixing process, and the crust thickness, but not surface tension, is also important

Lava Crust Formation

When a lava flow enters the ocean, a crust protects the hot fluid from rapid cooling There may be some additional cooling by water due to the formation of "pseudo-craters" and cracks opening at the time and place of crustal extension, but once a competent crust is formed, the heat loss from the crustal surface is, by and large, governed by the thermal conductivity of the crust and not by the rate of heat exchange at the lava surface The heat transport is described by a diffusion wave solution between a near constant temperature boundary and a semi-infinite region, the one water or atmosphere at $T \simeq 0$ to 50° C and the other hot lava at $\simeq 1{,}100°$ C The error function solution to the boundary value problem of thermal diffusion results in an effective "skin depth", the width of the thermal wave of

$$\delta = \sqrt{Dt} \text{ cm} \qquad (1)$$

where $D = K/C_v$ and where δ is the crust thickness, C_v the heat capacity per unit volume, K the thermal conductivity and t the time C_v is of order unity in c g s units—corresponding to a heat capacity of approximately 1/4 calorie g^{-1} $°C^{-1}$ and a density of 2 8 g cm^{-3} (ref 7) The thermal conductivity is approximately 5×10^{-3} calories cm^{-2} s deg^{-1} cm^{-1} (ref 8) The diffusivity, $D = (K/C_v) \simeq 10^{-2}$, and the thermal skin depth in a week ($t = 10^6$ s) becomes $\delta = 100$ cm The similarity solution, equation (1), assumes only that the outer boundary is a constant, T_1, and that the inner boundary asymptotically approach T_2, and although an outer boundary temperature T_1 in contact with seawater might be slightly cooler than an atmospheric boundary, this difference in outer boundary temperature is trivially small compared with the difference $T_2 - T_1 \simeq 1\ 1 \times 10^3$ °C

Therefore the crustal layer is thin compared with the thickness of the lava flow which may be 5 to 10 m thick on land and 20 to 60 m thick under the ocean[9] Nevertheless, for relatively slow lava motions, which typically are less than 100 m d^{-1}, the crust effectively shields the lava from any violent mixing Small eruptions, called pseudo-craters, may occur in a lava flow over ocean bottom, lake, or stream beds, but presumably these occur due to build up of pressure from the heating of a pocket of trapped water (Fig 1)

A more catastrophic release of energy is conceivable if ocean water and a large undersea lava flow were to mix autocatalytically Autocatalysis in this case implies that the pressure energy released by a given volume of water and lava is great enough to cause the further mixing and subsequent energy release of at least a slightly larger volume In this fashion an exponential type of reaction takes place that increases until limited by depletion of the reservoir The critical question is whether or not the gain is greater than unity because this determines whether an initiating disturbance grows or decays away

Underwater Explosions

When an explosive is detonated underwater, a shock wave propagates radially as a strong impulse of short duration that tends to fracture brittle objects, but does not significantly disturb semifluid media like sand or mud[10] Behind the shock wave is a region of high velocity fluid flow that is uniformly

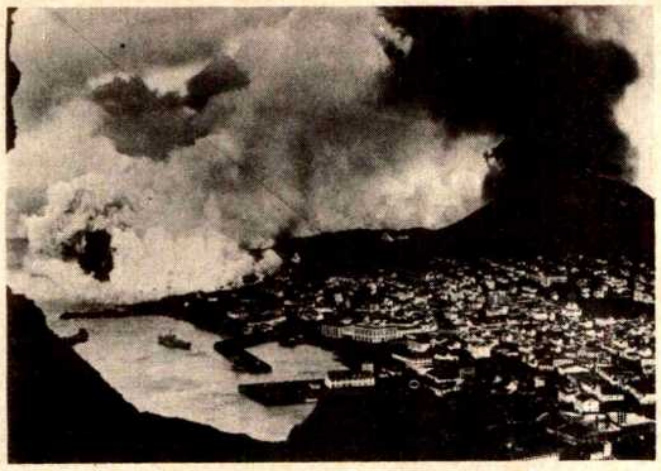

Fig. 1 Lava flow, volcano and town of Heimaey during the winter of 1973 is shown during the eruption of the volcano south of Iceland. The lava flow is entering the ocean and threatens to block the harbour entrance to the left. A pseudo-crater eruption is visible near the lava front where steam and finely divided lava are blown into the air as a grey cloud. We suggest that these small eruptions occur because of the entrapment of water beneath the flowing lava. Long[1] also suggests that the entrapment of water beneath molten aluminium poured into water is the mechanism for triggering his experimental explosions. (Photograph courtesy of Sigurgeir Jónasson and Icelandic Photo and Press Service.)

radial unless there is an interface present, such as that between ocean and ocean bottom. The flow velocity is larger in the less dense medium and by both the Helmholtz instability due to velocity shear, and Taylor instability from the acceleration of the heavy fluid by the light one, the light fluid penetrates the more dense medium and a mixture of mud, sand, rock, and water is ejected.

The quantity of sediment blasted free is almost always several hundred times the mass of explosive, and is roughly double the mass corresponding to a refilling of the crater void. The exact ratio depends on the details of the ocean sediments, but it holds within a factor of 2 from the smallest explosions to the largest nuclear bombs, provided only that the explosion is "stemmed" with the appropriate water depth in the ocean, or buried at the appropriate "scaled" depth on land[12–14]. The criterion for excavation of soils, sand, and mud seems to be that the dynamic pressure of fluid flow must be large enough readily to interpenetrate the material. The lower limit to the pressure at which most of this interpenetration takes place seems to be determined by the dynamical pressure of the matter at the outer limit where cratering ceases and where the bulk of the material that is removed, or mixed, in the explosion resides. This dynamical pressure is simply the energy released by the explosive divided by the mass of material in motion with some modest correction for the inefficiency of energy transfer. For typical explosives, including nuclear, roughly half of the energy is left behind in heat, so that per gram of standard "high explosive", 2×10^{10} erg is distributed in 200 g of cratered material. This results in an energy density of 10^8 erg g^{-1} of ejected matter, corresponding to 100 atm of dynamic pressure. The velocities at this point are subsonic, roughly 10^4 cm s^{-1} or 1/20 the speed of sound in solid matter. Therefore, the mixing in cratering occurs well after the initial shock has passed.

Explosive Equivalence of the Heat of Lava

The question of explosive mixing depends on whether the energy and pressure released in mixing is sufficient to cause the rapid further mixing of a still larger mass. The energy released when 1 cm^3 of lava at density 2.8 is cooled from a typical, 1,100° C to 100° C is approximately 2.8×10^3 J—0.44 of which is released in the detonation of 1 cm^3 of explosive of typical density of 1.6. Not all the heat of the lava is available to produce the PdV work that produces the typical cratering. If only a small amount of water comes in contact with a much larger mass of lava, the temperature, and hence pressure, of the steam will be very large, but only a small fraction of the heat will be removed from the lava, and the equivalent explosive mass will be small. At the opposite extreme, if a very much larger mass of water is mixed with the lava, a large fraction of lava heat will be invested in heating the water.

At temperatures above the critical temperature the latent heat of vapourization is continuous and a smaller fraction of the pressure energy, but at lower temperature, the latent heat is equal to or greater than the sensible heat in the steam. The optimum temperature for converting the lava heat to a form that can produce pressure times volume work will be somewhat above the critical temperature, where $T_c \simeq 370°$ C. We envisage the initial mixing to proceed sufficiently rapidly that the pressure wave cannot reach the free surface of the water in the time of initial heating and hence the initial pressure should correspond to water at $\rho \simeq 1$ g cm^{-3} and $T \sim 400°$ C. From Clark[8], $P \simeq 6{,}000$ atm. If we include the compressibility of an equal mass of adjacent cold water, then $\bar{\rho} \simeq 0.9$ at ~3,500 atm. The high pressure should lead to rapid further mixing of lava and high temperature water with subsequent expansion to the pressure of 100 atm corresponding to the cratering limit. The minimum heat requirement corresponds to maintaining the superheat of the steam at $T = 400°$ C. The enthalpy including the heat of vapourization and referred to 20° C is 720 calories g^{-1} (ref. 15). The mass of water required per unit mass of lava can be calculated by equating the respective heats

$$m_1 H_v = m_2 C_L (T_L - T_v)$$

where m_1 is the mass of water; H_v the enthalpy ($\simeq 720$ calories g^{-1}) at T_v, the vapour temperature (400° C); m_2 the mass of lava; C_L the heat capacity of lava (~0.25); and T_L the initial lava temperature (~1,100° C).

For these conditions, $m_1/m_2 = 1/4$. This is somewhat less than equal volume. Equal volume is roughly what is expected from the non-linear limit of growth (amplitude equals wavelength) of Taylor and Helmholtz instabilities when a final state of turbulence is reached. Taking into account the decreasing density of the water and steam, the ratio of $m_1/m_2 \simeq 1/4$ is reasonable, but it should be recognized that the mixing ratio should vary continuously from all lava to all water. We are concerned with estimates of the explosive effectiveness of the optimum ratio and ask even then whether autocatalytic mixing is likely.

Explosive Energy Equivalent

The energy released by a high explosive is not all available for performing PdV work at pressures above the cratering pressure of 100 atm just as will be the case for the superheated steam discussed previously. But the combination products of high explosive contain a significant fraction of H_2O as well as other molecules of N_2 and CO_2 that have a similar equation of state. Therefore, as a first estimate before detailed calculations can be performed, we compare the explosive effectiveness of high explosive and the water-lava mixture on an energy basis only.

The mass of lava that results in a quantity of steam at T_v equivalent to the energy content of 1 g of high explosive is

$$m_2 = \varepsilon_{ex}/(C_L(T_L - T_v)) = 5.2 \text{ g}$$

where ε_{ex} = specific energy released from high explosive = 10^3 calories g^{-1}. The initial pressure of 4,000 to 6,000 atm is forty times larger than the criterion for the upper limits of cratering so that the additional mass of lava mixed with water per unit of equivalent high explosive should be the multiplication factor $200/m_2 = 40$. This factor is sufficiently greater than the value unity required for self-sustained mixing that only relatively modest or inefficient mixing is required to maintain the reaction. The remaining question is whether the pressure of reaction can result in a configuration that ensures further mixing.

Mixing

Mixing requires that the lava and water interpenetrate each other to an extent such that the particle size is small enough to exchange the heat content of water and lava within the time of dynamical mixing.

Actually, only a very small fraction (1/40 of the water and lava) needs to exchange heat energy in order to self-sustain the mixing and then, once mixing has initiated an "explosion", a further heat exchange can take place during the very much longer time of expansion of the whole mass in the atmosphere. But in order to understand the limiting lava particle size required to self-maintain mixing of the initial smaller fraction, we assume that once the pressure is relieved by expansion of the free surface of the water, the dynamical mixing described by the cratering processes would be terminated. Therefore, choosing the marginal condition at $P=100$ atm, the time becomes $t=h/U_{\text{exp}}$ where $\rho_{\text{water}}U_{\text{exp}}{}^2/2=10^8$ dyne cm^{-2}, and where h = water depth; U_{exp} is the expansion velocity and so at $h=30$ m water depth, $t=0.2$ s. The upper limit to the lava particle size (or conversely water drop size) necessary to allow 50% heat transfer in this time is determined from equation (1) and results in the mixing condition that $\delta \leq 4\times10^{-2}$ cm, or a diameter $\leq 3\delta \simeq 0.12$ cm.

This is probably not highly restrictive because:

(1) The ash ejected by the degassing or "venting" of the hot magma as it decompresses at the atmospheric surface of a caldera occurs just in this particle size range.

(2) Many photographs of the more modest lava-water eruptions show a "grey" ejecta of steam and lava made up of millimetre size particles of lava carried by a jet of steam.

(3) Ash rings of small "shards" of volcanic material are found surrounding submarine eruptions and are formed "as a result of secondary steam explosions from a volcanic eruption underwater"[16].

(4) The material from large volcanic explosions is so finely divided that, in the case of the Krakatoa explosion, millions of tons of micron size particles remained suspended in the upper atmosphere for a year[9].

The way in which the lava is so finely divided is harder to justify.

Instabilities

Several well known instabilities lead to the mixing of two initially separated fluids that are set into relative motion. The first is the Rayleigh-Taylor instability that occurs when the two-fluid boundary is accelerated from the lighter fluid towards the heavier fluid. In this case, "tongues" of the two fluids interpenetrate each other. The next higher order of fluid instability, the Helmholtz instability, occurs on account of a differential shearing motion between the two fluids. In this case, waves are caused to grow to the point of breaking in a manner similar to ocean waves driven by the wind, but without gravity to hold the waves "down". Finally, a still more complicated phenomenon must occur at the water-lava interface due to the sudden chilling, solidification, and finally cracking or "spalling" of the fractured surface. Such a spalling occurs when molten glass is plunged into cold water. The first two fluid instabilities are complicated by the presence of the relatively high viscosity of the lava; the spalling instability depends upon the complexities of dynamical thermal stress and fracture propagation.

The Rayleigh-Taylor instability takes place at the interface between two fluids of differing density when the lighter fluid accelerates the heavier one. The growth rate ω of a perturbation of wave number $k=\pi/\lambda$ is:

$$\omega=[(\rho_2-\rho_1)/(\rho_2+\rho_1)gk]^{1/2} \tag{2}$$

where g is the acceleration.

The exponential growth (linear phase) is less important for our considerations than the non-linear phase of spikes of low density fluid interpenetrating the heavy fluid and bubbles conversely. Chandrasekhar[17] has shown that this phase of growth is limited by viscosity, ν, such that the shortest wavelength to grow rapidly is:

$$\lambda_{\text{min}} \simeq 70^{2/3} g^{-1/3} \nu^{2/3} \tag{3}$$

We can derive this expression approximately by saying that growth is limited when the viscous diffusion ($D=\nu/\rho$) is substituted in equation (1) for the diffusivity D, and the time, t, is taken as $1/\omega$ from equation (2).

If we consider mixing when the disturbance is of the order of the wavelength of the interpenetrating finger or bubble, then

$$g \simeq P/(\rho_L\lambda) \sim 10^9/\lambda \text{ cm s}^2 \tag{4}$$

where $P \simeq 3{,}500$ atm for the water before expansion. When we substitute this in equation (3)

$$\lambda_{\text{min}} = 2\times10^{-3}\ \nu \text{ cm}$$

The viscosity of lava on the small scale and of 1,100° C ranges from 10^3 to 10^5 (ref. 18) so that wavelengths of 1 to 100 cm are indicated. Similarly in the case of molten metals, the viscosity is of the order 1 c.g.s. unit so that fine scale mixing readily occurs.

The Helmholtz instability depends on turbulence to give rise to the mixing once surface waves have begun to grow. Turbulence is limited by viscosity in a fashion that is expressed by the requirement that the Reynolds number of the smallest eddy, or by analogy the shortest wavelength, must be greater than 100. The expression for the minimum wavelength becomes

$$Rey = 100 = \lambda_{\text{min}} U_s/\nu \tag{5}$$

where U_s is the velocity differential across the boundary. If we choose U_s to be its maximum value of 10^4 cm s^{-1}, and $10^3 \leq \nu \leq 10^5$, then λ_{min} lies in the range 10 cm to 10 m, roughly the same as the Taylor instability case. Again, the same argument applies to molten metals. The combination of these two instabilities occurs when the interpenetrating tongues of the Taylor instability are eroded by the Helmholtz instability.

Daly[19] has shown by numerical methods the progressive non-linear growth of the combined Rayleigh-Taylor and Helmholtz instabilities and confirms the Chandrasekhar theory. The distance the average interface between lava and water moves in the time for the minimum wavelength instability to grow several e folds in amplitude becomes the time for the surface to translate a distance of several wavelengths, so that the interpenetration occurs at roughly the same rate as the translation of the interface. Therefore, even if we assume that the viscous "strength" of the lava is high, the unstable Taylor and Helmholtz mixing should take place in dimensions small compared with the thickness of the lava flow. To achieve the fine scale mixing necessary to give the particle size $\lambda \sim 0.1$ cm, we must rely upon the "failure" of the partially crystalline structure of the cooling lava. The fine scale spalling analysis is uncertain; however, it is abundantly evident that such fine scale breakup of the lava occurs in any volcanic eruption even where the pressures are small compared with an atmosphere[9].

Geometry of Instability

Finally, we envisage a geometry where an initial pressure release at the lava-water interface is large enough to "crater" the crust and start a pressure wave radially along the interface. The pressure wave will travel faster in water than lava; hence, an annular high pressure region will push down on the lava, accelerating it downward and back toward the rarefaction at the original initiation point. The downward and radially inward acceleration of lava-water interface is both Taylor unstable as well as Helmholtz unstable from the velocity shear and should cause a major interpenetration and mixing of both fluids. Full mixing of optimum masses should give rise to a forty-fold gain so that very much less stringent conditions are possible yet still give rise to an explosive release of energy.

Minimum Size Perturbation

The minimum perturbation required possibly to initiate self-sustained mixing is of some interest. The initial disturbance should be sufficiently large that it "craters" a volume that penetrates the crust by a substantial fraction. If the crust is 1/3 m thick after a day, then the volume cratered should correspond to a hemisphere of radius roughly 2/3 m, or ~ 1 ton. If we assume a somewhat smaller cratering ratio of 100, because of the crustal strength, then the minimum mass of high explosive might be as low as 10 kg.

The properties of a natural phenomenon that could trigger such a mixing reaction become more restrictive. The rapid mixing or cratering condition requires a dynamic pressure of at least 100 atm. It is unlikely that when water "pours" into a collapsed caldera the overpressure created by the near steady state mixing can be much larger that twice the hydrostatic head. This then requires a depth of the caldera of at least 500 m or circumstances of "plugging" that create the same pressure.

Few volcanic explosions give rise to an atmospheric shock wave (which would require the sudden release of at least 1 atm pressure), so the sudden release of 100 atm is fortunately a rare phenomenon. Similarly, the difference in equivalent yield between the usual volcanic explosions and the events of Krakatoa and possibly Santorini is striking. The energy yield of most repetitive volcanic explosions is of the order of 10 to 100 ton high explosive equivalent, possibly as much as 10^3 ton for the undersea eruptions of the Myozin-syo volcano[9] south of Japan, whereas the Krakatoa equivalent yield was 2×10^8 ton. Santorini may have been even larger. This suggests that two different mechanisms are involved.

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Molecular Organization in the Sarcoplasmic Reticulum Membrane studied by X-ray Diffraction

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Orientated preparations of rabbit sarcoplasmic reticulum vesicles give X-ray diffraction maxima to a resolution of 16 Å. The calculated electron density profile shows that protein is distributed very asymmetrically in the membrane.

THE membrane system of the sarcoplasmic reticulum (SR) regulates the contractile cycle of muscle filaments by the uptake and release of calcium ions[1-3]. Closed vesicles derived from the SR have been isolated in good yield from muscle homogenates and shown to concentrate Ca^{2+}, using ATP as an energy source, in conditions similar to those prevailing *in vivo*[4]. The vesicles contain protein and lipid, in a ratio of about 65 : 35 (ref. 5). Several groups have shown that a major protein component, approximately 100,000 in molecular weight, accounts for a fraction of the total protein variously estimated as 30 to 60%[6-8]. The isolated protein possesses Ca^{2+}-stimulated ATPase activity[6,9].

Electron microscopy of SR membranes reveals that the preparations contain vesicles ranging in diameter from 500 to several thousand angstroms[10]. Vesicles negatively stained with uranyl acetate and phosphotungstic acid (PTA) appear to show an outer layer of 30–40 Å "spikes" or "particles" project-

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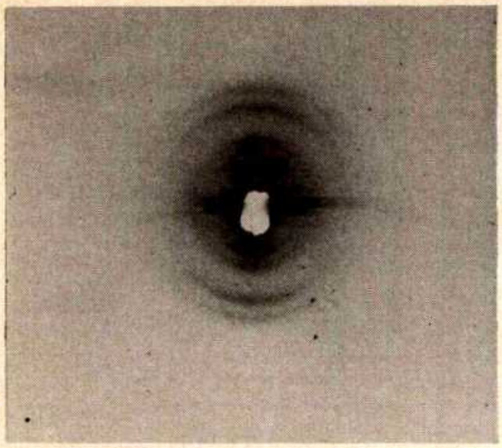

Fig. 1 X-ray diffraction photograph of orientated SR membranes. The second, third, fourth, sixth and seventh orders of a 234 Å repeat are visible. The orders 9, 11 and 13 can be seen on the original film. Equatorially orientated diffraction appears at 55 Å (just outside the position of the fourth meridional order). The photograph was taken with a mirror-monochromator point-focusing camera, used with an Elliott rotating-anode X-ray generator (focal spot 100 μm). The horizontal streaks are parasitic scatter from the quartz monochromator.

ing from the membrane surface, and freeze-etched preparations have somewhat larger (80 Å) particles in the plane of cleavage[11]. At least part of the ATPase molecule must be accessible from the exterior of the vesicle, as shown by ferritin active-site label experiments[10]. To define in greater detail the geometry of the SR membrane, we have prepared orientated specimens for X-ray diffraction. Our results show a distinct asymmetry in the organization of the SR membrane.

Orientated SR Vesicles

SR vesicles were prepared from rabbit skeletal muscle by standard methods[12,13]. We introduced an additional purification just before preparation of the X-ray specimen by centrifuging through a discontinuous sucrose gradient (Spinco SW65 rotor, 25,000 r.p.m., 2 h). The largest fraction was consistently found in a band between sucrose solutions of density 1.11 g cm^{-3} and 1.13 g cm^{-3}, and this fraction, dialysed against 0.02 M Tris-maleate, *p*H 7.2, 0.1 M KCl, 5% glycerol, was used for X-ray studies. Unfractionated vesicles gave identical diffraction patterns but with somewhat broader reflexions. Orientated specimens were obtained by centrifuging approximately 5 mg of SR (Spinco An-D rotor, 56,000 r.p.m., 12 h, 4° C) onto a mica strip, 1 mm × 12 mm, inserted into a 'Teflon' adapter at the bottom of a Beckman Model E analytical centrifuge cell. States of different water content were obtained by air-drying the 1 mm thick pellet in the cold for periods of up to 2 h. Coleman *et al.*[14] used similar techniques for orientating SR and other membrane preparations.

The specimens were cooled during X-ray exposure, and no change of spacing was observed for periods of up to 4 d. Enzymatic activity of the preparation survived the orientation, partial drying, and X-ray exposure, as shown by the data in Table 1. Ca-stimulated ATPase assays showed 80 to 100% specific activity in re-homogenized samples that had been dried to give X-ray spacings between 190 and 265 Å. Moreover, Ca^{2+}-uptake measurements indicated that a significant fraction of the re-homogenized vesicles were closed and capable of sequestering Ca^{2+}.

An X-ray diffraction photograph of the SR membranes (Fig. 1) shows along the meridian, orders of a single repeat whose spacing varies with the water content of the membranes. The diffraction generally extends to a resolution of 16 to 20 Å, depending on the state of the specimen. In many photographs we can detect traces of a meridional reflexion at about 60 Å, which becomes much stronger in very dry or maltreated samples. We attribute this line to an independent lipid phase, presumably from disrupted membranes. There are also rather diffuse equatorially orientated reflexions at 55 Å and in the 10 Å region. Our photographs are thus significantly better than those of Coleman *et al.*[14] who obtained only a few orders from centrifuged, dried SR membranes.

Table 1 ATPase Activity and Rate of Ca^{2+} Uptake in SR Membranes after X-ray Exposure

	X-ray spacing 190 Å	 240 Å	 260 Å
ATPase	0.8	0.8	1.0
Ca-uptake	0.3	0.5	0.7

Activities are normalized to the measured activity (taken as 1.0) of an equivalent weight of fresh SR membranes, before preparation for X-ray experiment.

See ref. 8 for methods.

Spacing and Water Content

The meridional spacing varies continuously from 270 Å for a freshly packed specimen not subjected to drying (50% water by weight) to 170 Å for a rather dry specimen (25% water). We observed altogether more than fifteen different spacings. In one case we obtained eight different spacings by successive dryings of a single specimen, an experiment which permitted us to follow all the reflexions and to ensure that no reflexions from lipid phases were included in our measurements.

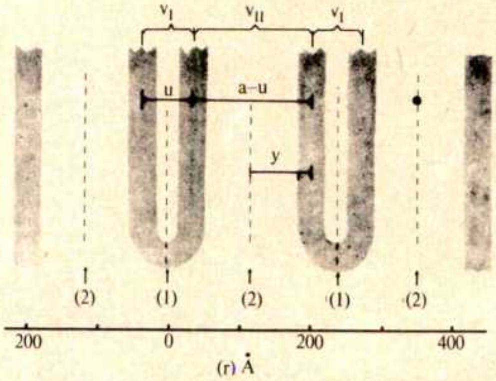

Fig. 2 Schematic diagram of packed vesicles. Considered in one-dimensional projection along the line perpendicular to the membrane planes, the distribution of matter has centres of symmetry between collapsed vesicles (2) and at the vesicle interior (1). The unit cell spacing is denoted by a and the two inter-membrane distances by u and a–u. The internal and external volumes v_I and v_{II} are shown to correspond to u and a–u, respectively. Evidence for this assignment is discussed in the text under the heading "Electron Density Profile." The scale at the bottom of the figure corresponds to a spacing a=234 Å.

The 170 to 270 Å repeat distance contains two apposed membranes; thus the line group of our one-dimensional unit cell has centres of symmetry. The shrinkage accompanying removal of water can in principle occur at either interface or at both—that is, at the vesicle interior or at the inter-vesicle surface (Fig. 2). Comparison of one-dimensional Patterson functions at different spacings indicates that over particular ranges of hydration, the shrinkage occurs in a relatively simple manner. The Patterson corresponding to a repeat distance a=234 Å appears in Fig. 3*a*. The peak at 37 Å remains essentially constant with spacing over the entire range; we attribute it to the inter-polar group vector (compare ref. 15). The strongest feature is the maximum at u=68 Å. If we ascribe this to a vector, **u**, between two membranes in a unit cell, then a–u=166 Å is the other inter-membrane distance (compare

Fig 2) Note that the separations u and a–u are very unequal, suggesting a difference in the inside–outside distribution of mass In Fig 2, we have shown **u** as the vector across the interior of a single collapsed vesicle (volume v_I) and **a–u** as the vector between vesicles (volume v_{II}) This assignment is at present arbitrary, but we indeed conclude below that there is more protein on the outer vesicle surface than on the inside and that the longer vector (**a–u**) must extend across the interface of apposed vesicles

The dependence of the distances u and a–u on the spacing a is shown in Fig 3*b* In the "wet" range $220 < a < 270$, u varies more rapidly than a–u In the "dry" range $170 < a < 220$, a–u changes, while u remains constant Within each range it should therefore be possible to trace a continuous transform by scaling diffracted amplitudes from specimens of different spacing In the "dry" range this approach will depend on the assumption that no significant structural changes occur within the shrinking volume v_{II}, and in the "wet" range by the further assumption that the slower variation of v_{II} may be ignored in comparison with the shrinkage of v_I We can evaluate these assumptions by analysing the continuous transforms themselves.

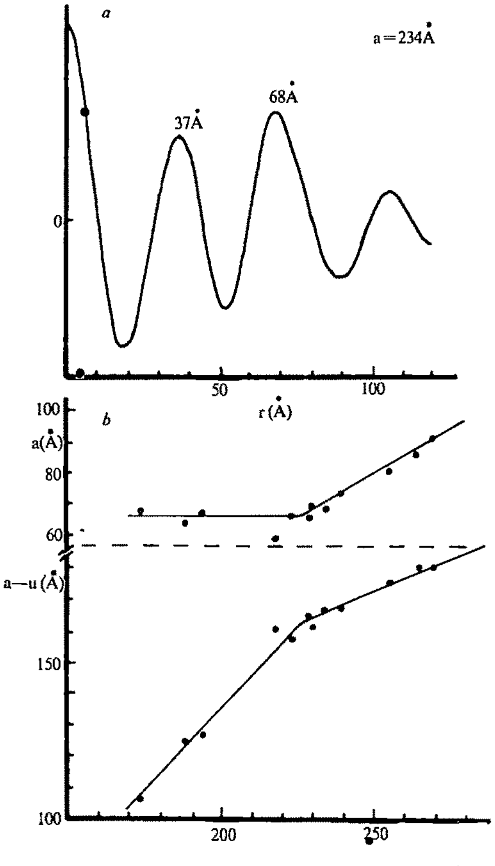

Fig. 3 *a*, One-dimensional Patterson function, calculated using intensities measured from the photograph in Fig 1 (a=234 Å) The photograph was photometered with a small beam along the meridian, and the F^2 (h) were obtained from the area under each peak by applying a Lorentz factor proportional to h^2 (as for a powder pattern) The internal and external volumes V_I and V_{II} are shown to correspond to u and a–u respectively *b*, Dependence of u and a–u on total spacing, a See Fig 2 for definitions

The transforms are shown in Fig 4 They consist of a series of alternating peaks and nodes Within each peak, the signs of all terms must be the same We can invoke the principle of minimum wavelength[17] and conclude that the signs of the first three peaks of the dry transform and of the first six of the wet transform must alternate The phases are thus determined to within an overall sign ambiguity to a resolution of about 30 Å We have calculated Fourier syntheses to resolve this ambiguity only one of the two sign sequences gives a plausible profile (Fig 5) It is not possible to continue the phasing in this manner, however, due to the broad region of low amplitude in the continuous transform near 0 0037 $Å^{-1}$ That is, the signs of the fourth and fifth maxima in the dry transform or of the eighth, ninth and tenth in the wet transform are undetermined with respect to the low resolution terms Within the region $0\ 04\ Å^{-1} < R < 0\ 06\ Å^{-1}$ the minimum wavelength argument again applies only an overall ambiguity of high-resolution signs with respect to low resolution signs remains unresolved With available data, we are unable to make a choice between the two alternatives

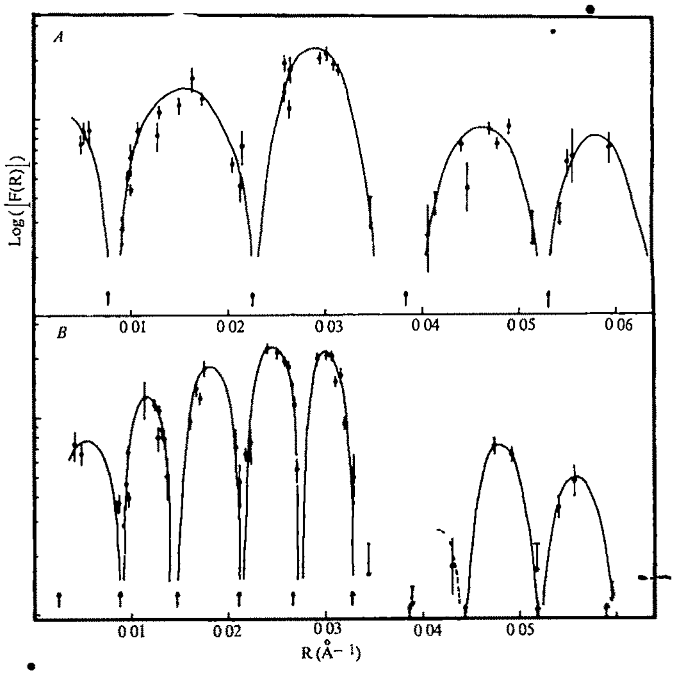

Fig. 4 Continuous transforms for SR membranes in wet and dry hydration ranges, derived by combining the corrected diffraction amplitudes corresponding to various spacings a The data for different spacings were scaled by normalizing the sum $\frac{1}{a}\sum_h h^2 I(h)$ for all reflexions between 0 and (30 Å)$^{-1}$ *A*, "Dry" transform $190 \leq a \leq 234$ Arrows indicate nodes of cos $2\pi(34)R$, *B*, "wet" transform $220 \leq a \leq 240$ Arrows indicate nodes of cos $2\pi(83)R$ We can understand the spacing of the nodes for each continuous transform by considering that the principal contrast in the electron-density variation across the membrane comes from the essentially centrosymmetric profile of a lipid bilayer, as in the treatment of the myelin structure by Caspar and Kirscher[16] We do not need to introduce the assumption of a centrosymmetric bilayer into our analysis We describe the continuous transforms in these terms here simply to make clearer the nature of their variation Let f(R) be the transform of this profile referred to an origin at its centre and let y and (a–y) be the positions of the membrane centres in the unit cell (compare Fig 2) Then the transform of the two-membrane structure, referred to the proper unit-cell origin, is $2f(R)\cos 2\pi yR$ In the "wet" range, it is appropriate to use centre of symmetry 2 (Fig 2) as the origin, since we take v_{II} to be approximately constant Then $y = 1/2$ (a–u) = 83 Å and the nodes of cos $2\pi yR$ are rather closely spaced, coinciding well with the nodes of the "wet" transform In the "dry" range, v_I is constant, and choosing centre of symmetry 1 (Fig 2) as the origin, we obtain $y = 1/2$ u = 34 Å Again, the nodes of the observed transform coincide approximately with the zeroes of cos $2\pi yR$

Electron Density Profile

Figure 5 shows the distribution of electron density across the SR membrane, calculated from the unambiguously-phased low-resolution reflexions The profiles for three different hydration states are given Their similarity is consistent with the arguments presented above, that no major structural changes occur on mild dehydration, and it is indeed this similarity that has been the basis of our approach to determining the structure An analogous method has been used in X-ray studies of myelin[16], and the comparison of different lattices containing identical structures is also a useful technique in protein crystallography[18]

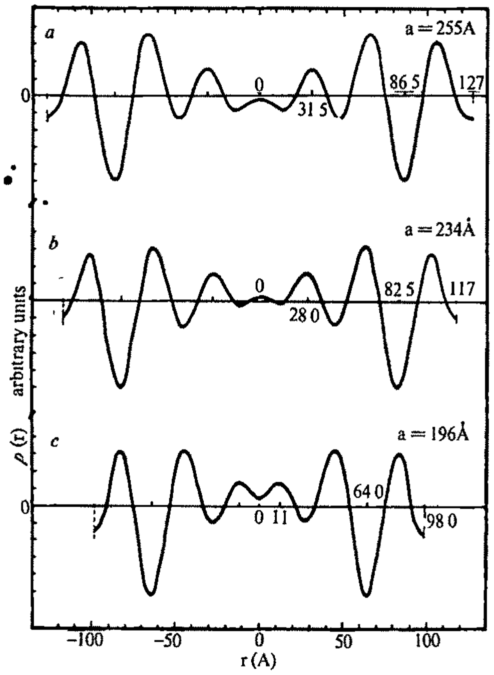

Fig. 5 Electron density distribution across the SR membrane Density in arbitrary units is plotted as a function of the distance, r, across the membrane The three profiles were computed to a resolution of 30 Å using the unambiguously phased reflexions, with signs indicated below *a*, a=255 Å +0−+0−++, *b*, a=234 Å +−−++−−+, *c*, a=196Å ++−++−−

An asymmetrically placed minimum is the most prominent feature of the SR electron density profile It indicates a bilayer organization of lipid in the membrane The maxima to either side are spaced about 40 Å from each other they show the position of lipid polar groups and associated protein (compare the low resolution profile of myelin) A density maximum appears at about 50–55 Å from the bilayer centre Its consistent appearance in all three profiles indicates that it is a significant feature, and not a Fourier cut-off effect It must represent protein that projects from one side of the membrane, and we can probably identify it with the projections seen in electron micrographs of negatively stained vesicles[11] This interpretation determines the inside and outside of the vesicle in our profiles It is presumably the projecting structure that gives rise to the large asymmetry in u and a–u (Fig 3*b*) The minimum inter-membrane distance observed on the external side with the projecting density maximum is about 110 Å, whereas the membranes can approach on the internal side to a distance of 66 Å

SR Membrane Organization

We have demonstrated that there is in the SR membrane a strongly asymmetric distribution of protein about a lipid bilayer The minimum in the electron density profile does not, however, imply that this bilayer be continuous Indeed, the composition of the SR requires that some protein penetrate—or dip into—the lipid We can see this by calculating the length fraction of the one-dimensional unit cell occupied by lipid The data in Table 2 show that one lipid bilayer has an "equivalent thickness" of about 26 Å Since the distance between polar groups estimated from the electron density profile is about 40 Å, the calculation implies that 30–40% of the volume in the interpolar group region contains either protein or water A model with either partial or complete penetration by the ATPase protein is clearly the most plausible The projections and the corresponding peak in the density profile could then represent either a tail of the ATPase molecule itself or a further protein component The magnitude of the electron density maximum suggests that it includes about 20% of the total membrane protein The reconstituted membranous structures obtained from purified ATPase show no projections[19], but the organization of the reconstituted structure cannot at this stage be assumed identical to the native

Table 2 Length Fractions of the Repeat Distance Occupied by Lipid, Protein and Water for Wet and Dry Orientated SR Vesicles

Spacing (a)	Water content (±5%)	Lipid	Length fraction Protein	Water
270 Å	50%	0 19	0 26	0 55
170	25%	0 30	0 41	0 29

The calculations are based on a protein lipid ratio of 65 35 and on the water content determined by weighing a sample before and after drying over P_2O_5 We assumed mean densities of 1 0 and 1 37 for lipid and protein respectively

Do our results provide constraints for describing the mechanism of Ca^{2+} transport in the SR ? The fact that we can record discrete meridional reflexions out to 15 Å resolution indicates that there is a relatively high degree of order across the membrane Moreover, the asymmetry of the structure is its most striking feature The ATPase molecules must therefore adopt quite uniform orientations and positions with respect to the lipid bilayer Isolation of the ATPase and restoration of activity by added lipid make it reasonable to assume that in the membrane this protein and associated lipid represent the entire functional transport unit[9,19,20] Since major translations or reorientations of the large ATPase proteins would require significant disruption of the asymmetric organization, our results favour a description of Ca^{2+} transport in which the transport system functions with at most relatively modest conformation changes

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LETTERS TO NATURE

PHYSICAL SCIENCES

Polar Cap on Europa

WE report here photoelectric observations of two occultations of Jupiter's satellite Europa (JII) by the satellite Io (JI). The reductions in the intensity during these events exceeds predicted values (K. A., unpublished) by 80% and 55% for the nights of June 17, 1973, and June 24, 1973, respectively. The durations and absolute times of occurrence are in close agreement with the predictions, indicating that errors in the orbital parameters or in the satellite diameters are not introducing large errors into the predicted light curve. We therefore conclude that Europa has a bright polar cap extending from the north pole to latitude ~30°.

The observations were made with a 61-cm telescope and a photon counting single beam photometer at the Mauna Kea Observatory. A cooled S20 photomultiplier tube and a Stromgren y filter ($\lambda_c = 5500$ Å) were employed. The sky signal was about 1% of the satellite signal for the 22 arc s aperture due to the large radial distance of the satellites (4.5 Jupiter radii) and the use of the freshly aluminized primary mirror. Sky readings were made ~13 arc s north and south of the satellites several times before and after each event and once during each event. Except for one instance of severe wind-loading on the telescope near the end of the event of June 24, variations in the sky signals were insignificant.

The observations of the event on June 17, 1973, are shown in Fig. 1. Each filled circle represents a 4 s integration. The predicted eclipse depth was 0.09 mag, based on satellite radii of 1,829.5 km and 1,550 km, and geometric albedoes of 0.80 and 0.72 for Io and Europa, respectively. The disks were assumed to have a uniform surface brightness. Because the observed eclipse depth is 0.17 mag, we have attempted to reproduce the light curve by decreasing the impact parameter, thereby increasing the fraction of Europa which is occulted. The dashed curve in Fig. 1 shows the predicted light curve if the satellite separation at mid-occultation is decreased by 400 km from the nominal orbit. Although the predicted depth of the eclipse (0.15 mag) is nearly equal to that which was observed, the predicted duration (260 s) is significantly longer than the observed duration (210 ± 10 s). The solid curve in Fig. 1 is the predicted light curve if the occulted portions of Europa have a geometric albedo of 1.30, while the average albedo remains 0.72. The duration (200 s), depth (0.17 mag), and the shape of the predicted curve closely match the observations.

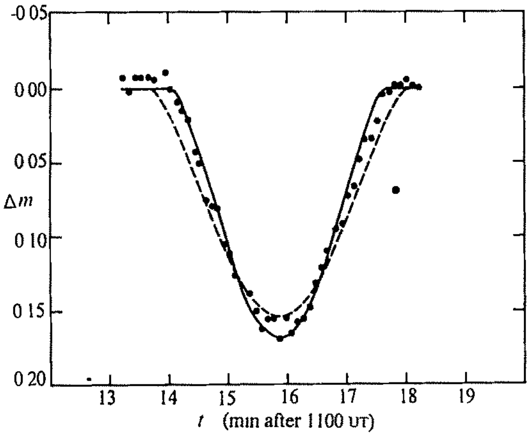

Fig. 1 Light curve for Europa occultation by Io on June 17, 1973, at 1116 UT. The predicted depth was 0.09 mag. Each filled circle represents a four second integration. ——, Light curve which results from the nominal orbital parameters but with the average geometric albedo of the occulted portion of Europa equal to 1.30 while the total geometric albedo of Europa is 0.72. - - -, Light curve which results from a modified orbit with the separation of the satellites decreased by 400 km but with Europa having a uniform geometric albedo of 0.72.

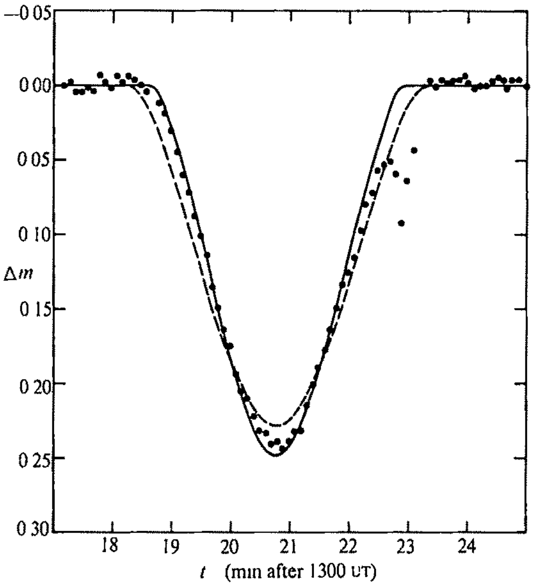

Fig. 2 Light curve for Europa occultation by Io on June 24, 1973, at 1321 UT. The predicted depth was 0.15 mag. The symbols are as in Fig. 1 except that —— represents the light curve for the nominal orbits and an average geometric albedo of the occulted portion of Europa of 1.12.

In Fig. 2 we show the observations of June 24, 1973, together with predicted light curves for the nominal orbital parameters with the satellite separation decreased by 400 km (dashed line), and for the nominal orbital parameters with the albedo of the occulted portion of Europa equal to 1.12 (solid line). As before the average albedo of Europa remains 0.72. The observations are marred by an excursion towards Jupiter caused by wind loading on the telescope, and it is difficult to assess accurately the duration of the event. The first half of the event required 120 ± 10 s, from which we estimate 240 ± 20 s for the total event. The nominal orbit yields a duration of 240 s while the modified orbit yields a duration of 290 s. The observed semi-duration is then in better agreement with the nominal orbit than with the modified orbit. It is clear that the observed depth, 0.24 mag, exceeds the nominal depth, 0.15 mag, and that it may be explained by a bright polar cap with an average geometric albedo of 1.12. The lower albedo of the larger occulted area on June 24 implies that the additional area occulted in this event is a mixture of high and low albedo material.

The existence of bright polar regions on Europa was suggested by the drawings of Lyot[1], who found Europa to be markedly different from the other Galilean satellites. The present observations confirm the correct nature of his drawings and indicate that very high contrasts are involved. Pilcher *et al.*[2] and Fink *et al.*[3] have shown that between 50% and 100% of the light from Europa is reflected from water ice. The exact boundaries of the polar cap cannot be specified from the present data alone, but we may estimate that it covers about 30% to 40% of the surface. With a similar polar cap in the southern hemisphere between 60% and 80% of the surface would be snow covered, and the remaining surface must necessarily consist of very low albedo ($0.0 < P < 0.1$) material such as that found by Murphy *et al.*[4] on the dark side of Iapetus. It is likely, however, that at least some of the discrepancy in the eclipse depths will be due to geometric factors. The extreme albedo values suggested there would then be moderated, but the concept of polar ice caps covering a low albedo surface is unlikely to change.

Complete mapping of this same face of Europa is possible if high quality photoelectric observations are obtained of the entire series of occultations of Europa by Io. All observers are urged to observe every event visible from their location and to forward their observations to the data bank c/o Dr R. L. Millis at the Lowell Observatory, Flagstaff, Arizona, United States. Detailed prediction of the events are available from several sources[5-7].

We thank Professor W. M. Sinton for discussions and Mr A. Lazarewicz, who made the observations of June 24, 1973. This work was supported by grants from the National Aeronautics and Space Administration and the Air Force.

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Praesepe and the Solar Neutrino Problem

Sagan and Young[1] have suggested that the solar neutrino problem and the apparent presence of river channels on Mars may both be resolved by variations of 10% to 20% in the solar luminosity, and they have cited the observed width of the main sequence in Praesepe as evidence that such luminosity excursions have occurred in other solar-type stars. But the main sequence width has previously been interpreted[2,3] as due to the observed spread in rotational velocity of the stars. Are these interpretations mutually exclusive or could they be compatible?

Using the data of Johnson[4], Sagan and Young found that the standard deviation for the main sequence stars in Praesepe with $0.3 \leq B-V \leq 0.6$ is about ±0.1 mag. I have obtained a similar, though slightly larger, result using more recent data[5]. Stars of later type show an appreciably smaller scatter. This result agrees qualitatively with the known facts that stars of earlier spectral type rotate faster on average[6] and that rotation moves a star upwards and to the right in a colour-magnitude diagram[7]. Thus the sample of earlier spectral type contains stars with a greater spread of rotation speeds and so a greater spread in magnitude.

Theoretical considerations[7] suggest that the vertical spread of the main sequence in magnitude, ΔM_V, is approximately related to the rotation speed v by the relation

$$\Delta M_V = \chi v^2$$

where χ is roughly constant along the main sequence for stars with a given angular momentum distribution. In units of 10^{-5} mag (km s^{-1})$^{-2}$, χ has the value 0.4 for uniformly rotating stars. Using the data of Dickens *et al.*[3,5], the root mean square velocity of stars in Praesepe with $0.3 \leq B-V \leq 0.6$ is about 100 km s^{-1} and so the expected standard deviation in magnitude if the stars are rotating uniformly is ±0.04 mag—less than half the observed spread. The previous interpretation of this result[2,3,8] has been that the stars must be rotating non-uniformly, though the data is not accurate enough to favour any particular rotation law[3]. On that interpretation, there is no need to invoke any further broadening mechanism, and the main sequence dispersion in Praesepe gives no support to the hypothesis of Sagan and Young.

But one could also argue that the stars are rotating uniformly—as seems to be the case for stars with $B-V < 0.3$ (ref. 9)—and that rotation contributes only ±0.04 mag to the observed spread. If the luminosity excursions required by Sagan and Young were only slightly less than they suggest, and gave a standard deviation of ±0.09 mag, the combined standard deviation would be the observed ±0.1 mag. An argument against this interpretation is that, as noted by Sagan and Young[1], the stars in Praesepe are distributed approximately uniformly within the main sequence band. This is consistent with the known, rather flat distribution of rotation velocities but is surprising if, as has been suggested[10], the ^{3}He mixing episodes last for a time short compared with the time between mixings.

I conclude that, although the evidence from Praesepe does not necessarily contradict the hypothesis of Sagan and Young, neither does it positively support it and it is possible to explain the entire observed width of the main sequence in a much less exotic way. Evidence for episodic mixing in solar-type stars must be sought elsewhere.

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Two Probable Astroblemes in Brazil

MORE than forty structures have now been identified as astroblemes, ancient geological scars produced by the impacts of large cosmic bodies on the Earth[1]. We report here some preliminary results on the study of two new astroblemes in Brazil, the Araguainha Dome and the Serra da Canghala structure. Although relatively young meteorite impact craters have been identified in Argentina[2] and Chile[3], these two Brazilian structures are the first ancient astroblemes to be reported from South America. The impact origin of the Araguainha Dome has been established by the discovery of diagnostic shock-metamorphic effects[4] in its rocks. No shock effects have yet been identified in rocks from the Serra da Canghala structure.

The Araguainha Dome, centred at 16° 46′ S, 52° 59′ W, is located near the town of Araguainha in the state of Matto Grosso, Brazil. The structure has been regarded as an alkaline intrusive, of which there are many examples in Brazil. It consists of a central uplift about 10 km across, in which cataclastically deformed Devonian Furnas Sandstone is exposed. Around this uplift is an annular ring syncline in which Permo-Carboniferous sediments, chiefly sandstones, are exposed in a series of downdropped grabens. The diameter of the structure estimated from ground studies is about 20 km. But a photograph of the structure taken from the ERTS-1 satellite (ERTS-1 photograph 1089-13005; October 20, 1972) shows that the circular pattern extends across a diameter of about 40 km (Fig. 1). If this pattern represents the true size of the structure, then the Araguainha Dome is one of the larger known astroblemes.

The central part of the central uplift is occupied by an unusual igneous breccia which contains inclusions of buried quartzofeldspathic Precambrian crystalline rocks in an igneous matrix. Thin sections of this breccia and the inclusions, made available to us by officials of Petróleo Brasiliero SA (Petrobras), contain a wide variety of distinctive shock-metamorphic effects, which are diagnostic of the intense shock pressures ($\geqslant$100 kbar) produced by meteorite impact. The inclusions show extensive development of planar features (shock lamellae) in quartz, often as many as six to eight distinct sets of lamellae per grain, with orientations corresponding to the distinctive $\{10\bar{1}3\}$, $\{10\bar{1}2\}$, $\{11\bar{2}2\}$, and $\{11\bar{2}1\}$ planes[5,6]. The igneous matrix of the breccia exhibits a heterogeneous texture and contains numerous shocked and partly melted rock and mineral inclusions. The breccia from the Araguainha Dome is identical in appearance to impact produced breccias observed at other astroblemes.

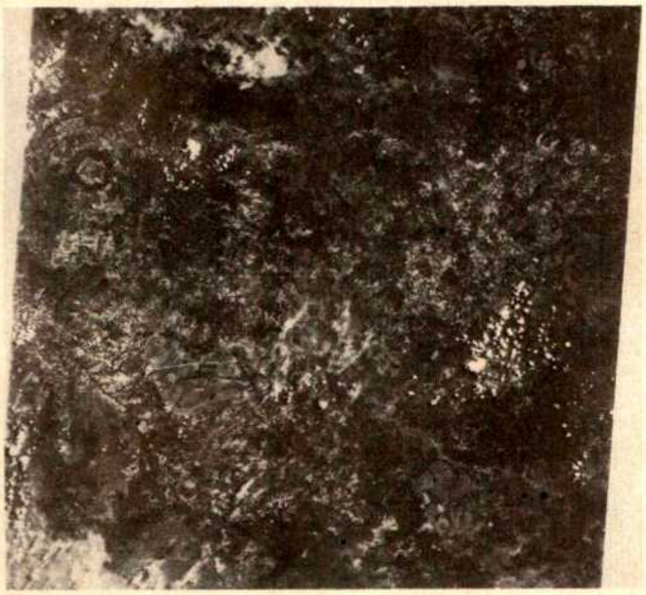

Fig. 1 ERTS-1 photograph of the Araguainha Dome. The structure appears at upper left as a dark inner ring and an outer circular pattern about 40 km across. NASA photograph, courtesy N. M. Short.

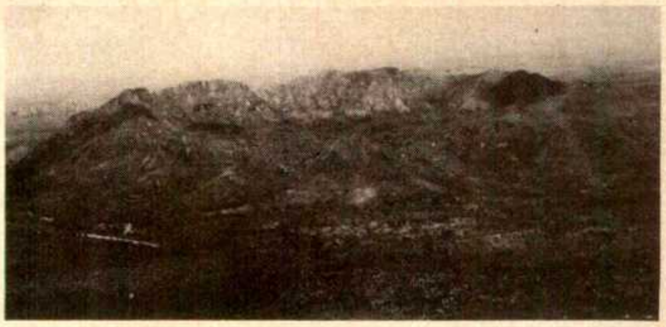

Fig. 2 Aerial photograph of Serra da Canghala structure, showing high wall of uplifted Poti Sandstone around the central uplift. Part of the downdropped ring syncline is in the foreground. White streak at left is an aircraft landing strip.

The Serra da Canghala structure ("Pack-Saddle Mountain") is located in the remote northern corner of the state of Goiaz (8° 05′ S, 46° 52′ W) in north-eastern Brazil, on the southern limb of the Amazon basin. The structure (diameter 12 km) has a damped-wave form with a central uplift of diameter 5 km surrounded by a downdropped annulus at least 3.5 km across. Serra da Canghala is a remarkably impressive feature of the region. In the central uplift, a circular wall, 250 m high, of steeply dipping Poti (Carboniferous) Sandstone surrounds a central basin of uplifted Longa (Devonian) Shale (Fig. 2). The central part of the structure thus has a crater-like apearance resulting from the preferential erosion of the Longa Shale by streams which flow through a breach in the Poti Sandstone wall.

In 1971 the Company for Research on Mineral Resources (CRPM) drilled three diamond drill holes, each 200 m deep, within the centre of the structure to test the possibility that the structure might be a kimberlite intrusion. No igneous rocks were found, and the drilling encountered only highly deformed and steeply dipping Longa Shale. The drilling results and the surface outcrop pattern indicate that the central uplift becomes progressively more disturbed towards the centre of the structure and displays the forms of an eviscerated dome. The intensely disturbed central area, the down thrown peripheral annulus, and the ratio of the central uplift diameter to total diameter are consistent with the structural features found in astroblemes. The overall structural pattern and geomorphology are strongly similar to those at the Gosses Bluff astrobleme in central Australia[7,8].

The rock units underlying the Serra da Canghala structure down to the Precambrian basement are entirely clastic and do not contain significant carbonate or salt units; the structure cannot be a salt diapir. Igneous rocks are entirely absent from the structure, and large cross-cutting sandstone dikes are the only anomalous features.

One of us (R. S. D.) made a three-day reconnaissance and collection at the Serra da Canghala structure in October 1972. Shatter coning, a useful field criterion for meteorite impact[9], was not observed. The rocks collected were almost entirely fine-grained siltstones which did not show any shock-metamorphic effects. One specimen of coarser grained quartzite, collected as a cobble in a conglomeratic unit of the Poti Sandstone in the central part of the structure, showed small areas characterized by unusual fracturing of the quartz grains. Similar fracturing in quartz has been reported in mildly-shocked rocks from known meteorite impact craters[10,11], but the features observed in the Poti Sandstone are not distinctive enough to be considered diagnostic for meteorite impact. At present, the structural deformation in the Serra da Canghala structure, combined with the apparent absence of igneous activity, favoure the theory that the structure is an astrobleme. But definite proof will require the identification of unquestionable shock-metamorphic effects in its rocks.

We thank the Company for Research on Mineral Resources (CRPM) for making possible the field work at Serra da Canghala and for providing the assistance of J.-M. Coehlo in the field. M. Antonio M. de Oliveira of Petróleo Brasiliero SA (Petrobras) provided the thin sections and information on the Araguainha Dome. Petrographic studies were carried out at NASA, Goddard Space Flight Center, courtesy of C. C. Schnetzler. N. M. Short, also of NASA, Goddard, provided information and ERTS photographs of the Araguainha Dome. Partial support for R. S. D.'s travel to South America was provided by the Barringer Crater Co., Philadelphia, Pennsylvania.

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Evidence of Features in Atmospheric Spectra at around 8 cm^{-1} of Probable Solar Origin

OUR studes of emission spectra of the stratosphere in the frequency range 30 to 200 cm^{-1} from a Caravelle[1,2] have revealed lines due to the principal atmospheric components H_2O, O_2 and O_3.

The flights were made during night and day and the spectra were then compared in order to identify the possible existence of photoreactions or other phenomena induced by the Sun. An unexpected feature always appeared in the day spectra around 8 cm^{-1}, but never in the night spectra (Fig. 1). This could not be due to some instrumental artefact, and effectively laboratory spectra do not show any anomalous peak in this spectral region.

Outside the frequency range 30 to 200 cm^{-1} the spectral response is negligible, so the signal we detected cannot reasonably be attributed to any atmospheric spectral feature. On the contrary, because Fourier transform techniques are used, time fluctuations of the atmospheric background may cause the kind of features that we observe. Actually, the interferogram contains information not only about the spectral distribution of the energy but also about its time fluctuations. In our case each step is either 20 μm in optical path difference or 0.850 s in time. We have carried out a power analysis of the signal to determine its time characteristics. The interferograms have been convolved with a low pass filter reducing, in the spectral band of interest, the contribution of the noise coming from the remaining part of the frequency band. Three power spectra of consecutive interferograms are shown in Fig. 2. The measurements were done at an altitude of 11.6 km with a spectral resolution of 0.18 cm^{-1}. Strong peaks appear at 20.31 and 21.25 mHz (*a*), 19.65 mHz (*b*), 17.4 and 19.65 mHz (*c*). The frequency resolution being 0.85 mHz, we note that the phenomenon causing the peaks is variable in time and in amplitude. Similar analysis of the night data shows no peaks of this kind. In addition, the shape of the power spectrum is fluctuating in time without any regular trend. Assuming that all the signal is essentially due to non-stationary atmospheric noise, we can determine its maximum amplitude in order to fix an upper limit to the confidence of the peaks in the daytime power spectra. These values are reported in Fig. 2.

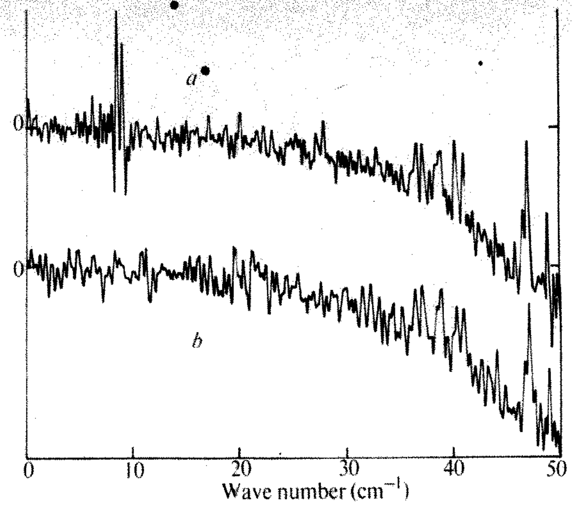

Fig. 1 Examples of two different emission spectra of the sky obtained at 12.5 km. The upper spectrum (*a*) was recorded during a day flight and shows a large feature around 8 cm^{-1}. The lower spectrum (*b*) was recorded in the night flight subsequent to that in which spectrum *a* was recorded and does not show any evidence of similar peaks.

Independent measurements on atmospheric noise have been performed by one of us (N. E.) at the Cassegrain focus of the 60-cm Meudon Observatory telescope with a helium cooled bolometer in the atmospheric window 8–12 μm. The experiment was performed on March 2, 1973, with a sky totally free of visible clouds. The emission measured with a 16 arc s beam had a signal to noise ratio of 140. Periodic oscillations of the signal with an amplitude of 4% that of the sky signal were observed. The power spectrum analysis of these data in the range 0 to 1 Hz with a resolution of 5 mHz shows the existence of three maxima at 7.5 mHz, 15 mHz and 26 mHz (Fig. 3). There is good coincidence of the frequency of the last two peaks with those found in the airplane spectra, obtained without any telescope and with a beam aperture of 14 arc deg.

Atmospheric transmission measurements by Biraud *et al.*[3], between 300 μm and 1 mm, show in the solar spectrum an absorption peak around 8 to 9 cm^{-1} which does not appear during night measurements on the Moon (Fig. 2 of ref. 3). Similar observations have been carried out by Nolt *et al.*[4] in two frequency bands. In the 7 to 40 cm^{-1} band a feature with an apparent shape like that in our spectra is seen at about 8 cm^{-1} (Fig. 3 of ref. 4). From the experimental parameters given in ref. 4 we conclude that this feature corresponds to frequencies of 50 to 60 mHz. In addition, in the 5 to 20 cm^{-1} band a broad absorption occurs between 8 and 10 cm^{-1} Further support comes from refs 5 and 6 Although the experimental conditions were different, anomalous absorption peaks at 7 3 cm^{-1} and 9 3 cm^{-1} are observed in the solar spectra which cannot be attributed to known minor atmospheric constituents The difference between the mean absorption observed and that expected from theoretical calculations is a factor of ten In addition, there is evidence for sky emission features at the same wavelengths at which the anomalous absorption appears

We note that if the phenomenon which produces the features is time dependent, the peaks may appear everywhere in the submillimetre range, with a frequency defined by the experimental parameters, the length and the duration of the repetition time of each step of the interferometer moving mirror Obviously frequency ranges in which no spectral lines are expected give better evidence of the peaks, whereas in the regions where lines occur, the feature may be superposed on the real spectrum affecting both the line intensity and shape[7] Evidence of this is given by the work of Mather *et al*[7] who have detected sky emission between 6 and 14 cm^{-1} using a Fabry-Perot which operates in a different way from a Michelson interferometer The expected consequence is (Fig 2 of ref 7) that no emission features emerged from the noise level in the frequency range 7 5 to 10 cm^{-1}

The phenomenon which produces this feature both in airplane and ground spectra is fluctuating in amplitude and in time (periods from 20 s to 140 s), and its appearance only on day records reasonably suggests a solar origin On the other hand, the fact that it is detected in both solar absorption and emission indicates that the source must be very large The airplane measurements at about 1 km above the tropopause prevent any possible attribution to tropospheric fluctuations such as those studied by Kazès and Steinberg[8]

The solar chromosphere, at centimetre and millimetre wavelengths has quasiperiodic pulsations correlated with the solar activity The frequency of these fluctuations changes time with time with periods varying from 12 to 170 s (refs. 9–11)

The similarity of these periodicities with those found in our spectra suggests to us that these fluctuations may be attributed to the anomalous feature that we observe On the other hand, the isotropy of the signal in emission suggests that the chromospheric quasiperiodic fluctuations must be coupled to the Earth through a medium able to produce this effect, such as the ionosphere

We also note that the phenomenon we have identified has important consequences for the correct interpretation of far infrared atmospheric and astronomical data To this end, further measurements are in progress

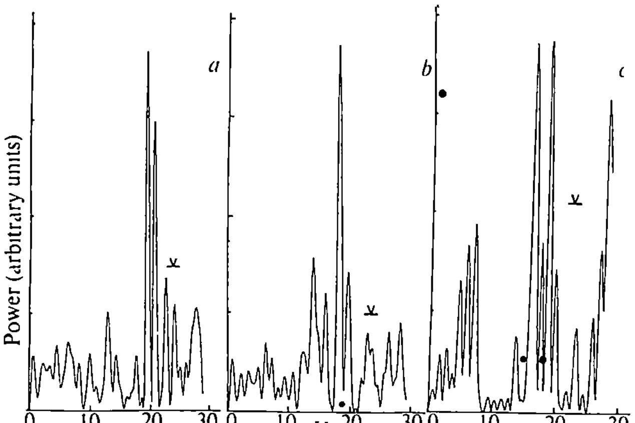

Fig. 2 Power spectra of the signal in three consecutive day measurements Strong peaks appear respectively at *a*, 20 31 and 21 25 mHz, *b*, 19 65 mHz, *c*, 17 4 mHz and 19 65 mHz The peak noise amplitude obtained from night power spectra (see text) is shown by the arrow

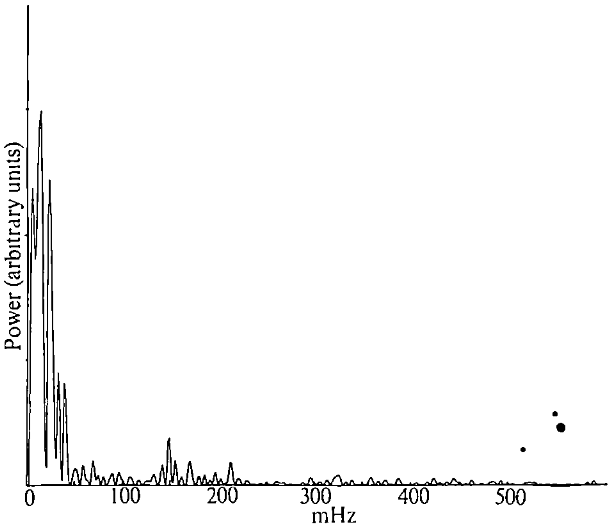

Fig. 3 Power spectrum of the sky noise data recorded on March 2, 1973, at the Cassegrain focus of the 60-cm, *f*/12 5 Meudon Observatory telescope Three strong maxima fall at 7 5 mHz, 15 mHz and 26 mHz

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Caribbean Climate during Pleistocene Ice Ages

IT is a matter of controversy whether during Pleistocene ice ages non-glaciated intermediate and low latitude regions of the Earth were subjected to humid (pluvial)[1,2] or to arid climates[3–5] We present here data on Pleistocene climates of the Caribbean basin, which may help clarify this question

We examined a deep sea sediment core collected from the central part of the Caribbean Sea (core P6304–9, 14° 57′ N, 68° 55′ W, water depth 4,126 m) A detailed $^{18}O/^{16}O$ palaeotemperature curve for this core indicates that it contains an undisturbed record of the late Pleistocene[6] The isotopic palaeotemperature variations along the length of the core (Figs 1, 2) reflect oscillations in the temperature of seawater, which in turn are related to Pleistocene climatic fluctuations

Other parameters measured in this core[6-9] all show cyclical variations which correlate closely with the palaeoclimatic oscillations

Selected portions of the core (0 to 500 cm and 700 to 900 cm) were sampled each 10 cm, the calcium carbonate fraction of the samples was removed by treating the sediment at room temperature with a 0 5 N solution of acetic acid The mineralogy of the carbonate-free sediment was determined by X-ray diffraction, using a General Electric XRD-5 diffractometer with Ni-filtered CuKα radiation Excluding biogenous calcite, the principal minerals contained throughout the core are quartz, kaolinite, micas, plagioclase feldspars, and smectites

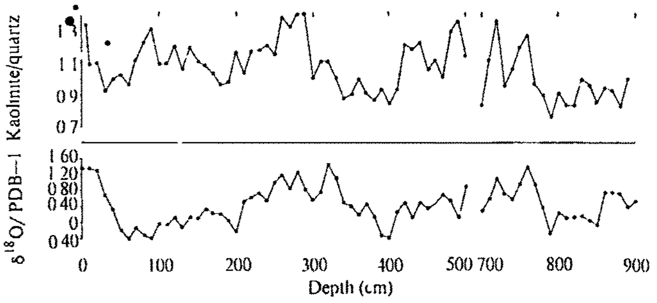

Fig 1 Variations in the kaolinite/quartz ratio in the 0 to 500 cm and 700 to 900 cm interval of core P6304-9 compared with the $\delta^{18}O$ palaeotemperature curve

In Fig 1 we show the variation with depth in two sections of the core of the ratio (in concentration) of kaolinite to quartz In the present context we believe that this parameter can be used as an indicator of palaeoclimate Kaolinite is a layered silicate commonly produced by chemical weathering under very humid climatic conditions At present it is the principal clay mineral formed in humid tropical and equatorial continental areas such as in the lower basins of tropical and equatorial rivers of western Africa and South America[10-12] Quartz, on the other hand, is resistant to chemical weathering and is transported into marine basins mainly from arid lands, largely through the atmosphere[13,14] Thus, one would expect the kaolinite/quartz ratio to be higher in Caribbean sediments during periods of increased humidity, and lower during periods of increased aridity

The ratios of the intensity of diffraction lines characteristic of the two minerals were measured, such ratios are proportional to the actual ratios of the concentration of the two minerals We measured the ratios graphically, using the (001) reflexion of kaolinite at 12 4° 2θ (CuKα) and the (100) reflexion of quartz at 20 9 θ (CuKα), with the following instrumental parameters 35 kV, 25 mA, divergent beam slit 1°, convergent beam slit 0 2°, goniometer speed 1° min^{-1} The measured ratios are reproducible to within 5% Possible minor contributions of the (002) peak of chlorite to the (001) peak of kaolinite do not affect our conclusions

The kaolinite/quartz ratio in the 0 to 500 and 700 to 900 cm sections of the core displays some broad fluctuations (Fig 1) where broad minima (corresponding to periods of relatively high aridity) correlate positively with minima in Emiliani's[6] $\delta^{18}O$ curve, corresponding to cold climate stages Thus, we conclude that during Pleistocene cold stages (ice ages) conditions of relatively high aridity prevailed in the Caribbean basin, while more humid conditions prevailed during the interglacials

Examination of samples from core P6304-9 with a high power optical microscope revealed the presence of mineral plates 3 to 4 μm in diameter, with polygonal outline and very weak birefringence Electron micrographs (Fig 3), and X-ray diffraction analyses identified them as well crystallized plates of kaolinite viewed perpendicular to the (001) direction Their concentration was estimated at the microscope by comparison with area estimate charts each 10 cm along the length of the core (Fig 2) There is a clear correspondence between palaeotemperature maxima and the abundance of the platy kaolinites, bearing out the concept of increased humidity in the Caribbean region during warm climatic cycles (interglacials)

The maxima of the kaolinite/quartz ratio and of the concentration of platy kaolinite are displaced upwards a few cm relative to the $\delta^{18}O$ palaeotemperature maxima in some of the cycles (Figs 1 and 2) This could be explained if the maxima of humidity in the Caribbean basin followed the warm temperature peaks by a few thousand years, however, even if humidity maxima were contemporaneous with warm temperature peaks, the time required for chemical weathering of the circum-Caribbean regions, stripped of all chemical weathering products during the previous arid cycle, as well as for transporting the weathering products to the deep seafloor, may have resulted in a time delay between humidity maxima and corresponding maxima of the kaolinite/quartz ratio in the sediment

The decrease with depth in the core of the average concentration of platy kaolinite (Fig 2), and the lower average kaolinite/quartz ratio in the 700 to 900 cm section relative to the 0 to 500 cm section (Fig 1) may be explained by the instability of kaolinite in the marine environment, and may reflect the gradual breakdown of the large plates into finer kaolinite crystals during the earliest stages of diagenesis Further degradation of kaolinite may be slowed by burial and may take place at exceedingly low rates, possibly according to a reaction of the type kaolinite + K^{+} = muscovite Reactions of this type have been verified in the laboratory at relatively low temperature[15]

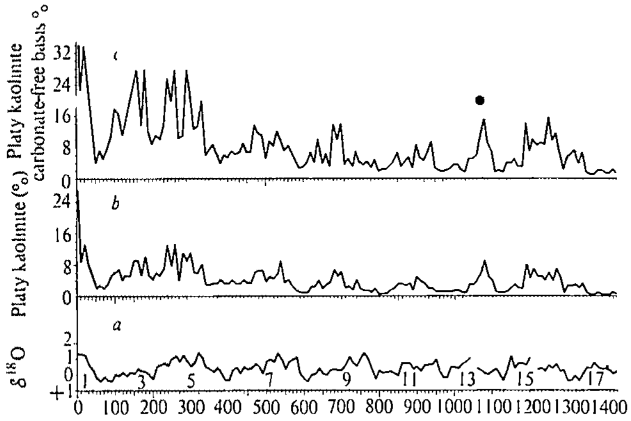

Fig 2 Variations in platy kaolinite with depth in core P6304-9 in relation to isotopically determined palaeotemperature *a*, $\delta^{18}O$ palaeotemperature curve (from Emiliani[6]), *b*, platy kaolinite as a percentage of the whole sediment, *c*, platy kaolinite as a percentage of the sediment on carbonate-free basis Recalculation on a carbonate-free basis was made using the $CaCO_3$ data of Bostrom[8]

Although our evidence cannot be applied to any one specific land area in the Caribbean region, we conclude that the provenance area of detrital sediments of the Caribbean was, in general, more arid during Pleistocene temperature minima than during temperature maxima The inferred increased aridity of the Caribbean region during Pleistocene Ice Ages is in line with data indicating ice age aridity in the western equatorial Atlantic as well as in tropical South America[10-12,16] Evidence of increased aridity during ice ages has also been found in equatorial and northern Africa[5] and in southern Europe and the Mediterranean[3,4] Thus, it is possible that the arid climatic belt around the globe expanded during Pleistocene cold periods both towards the equator and towards the middle

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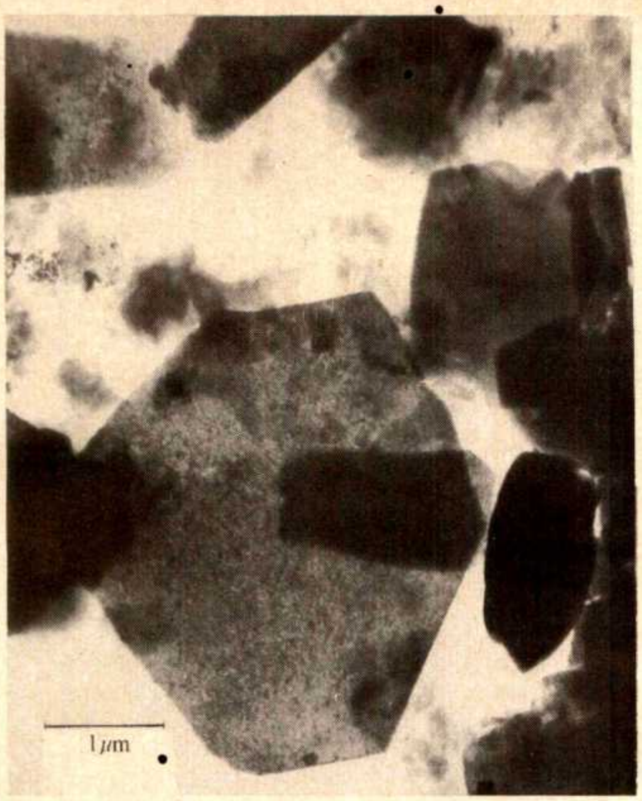

Fig. 3 Transmission electron micrographs of individual crystals of platy kaolinite from the 0 cm level of core P6304–9. The scale marker is 1 μm. Micrographs obtained with a Philips electron microscope.

latitudes. One factor which may have contributed strongly to this phenomenon is the decreased temperature of surface water of tropical and temperate oceans which would have reduced significantly the supply of water vapour to the atmosphere in these regions.

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Continental Drift, Magmatic Provinces and Mantle Plumes

REGIONS of magmatic activity on and in the Earth's crust have long been attributed to thermal "highs", hot spots or mantle plumes. Present doctrine[1-3] holds that these plumes have a fixed abode in the upper mantle, rising through the lithosphere from time to time, to "burn" holes in the crust. If the lithosphere happens to be moving as a result of active seafloor spreading, a so-called plume scar or plume trace is left in the crust, as a line of volcanoes or intrusive centres.

The thesis is useful for explaining some linear volcanic island chains, of which the best documented example remains the Hawaiian group (see ref. 3). But some recent applications of the idea to continental regions are invalid because of basic inconsistencies.

(1) The plutonic intrusions of New Hampshire (USA), the seamount chain off the New England coast, and the Azores archipelago have been linked[2,4] as products of a single mantle plume that first became active about 200 m.y. ago, when the North Atlantic began to open, and has continued to be intermittently active up to the present.

On this model, the 200 km long New Hampshire belt of some twenty igneous complexes, chiefly granitic (the so-called White Mountain magma series), represents the earliest phase of activity. The north-northwest trending belt is interpreted as a scar formed by movement of the North American plate over the plume, during the period from about 210 to 110 m.y. ago, corresponding to the range of radiometric ages determined for individual intrusions within the province[5].

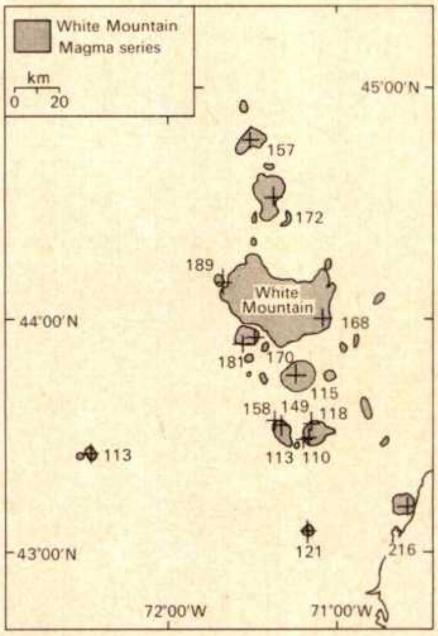

Fig. 1 Complexes of the White Mountain magma series with age data determined by Foland *et al.* +, Sample sites.

One of the axioms central to plate tectonic theory is that the direction of seafloor spreading from active ridge axes does not suddenly reverse itself nor undergo abrupt short term changes of direction through sharp angles. It follows that if the New Hampshire complexes do represent a plume scar, then they should become progressively younger towards the south-southeast. Figure 1 summarizes recently determined radiometric age data[5] and shows that this requirement is not met. There is no consistent pattern in the migration of centres. But the most fundamental inconsistency of this model lies in the overwhelming evidence from many sources (see ref. 6), that the North Atlantic was already about half its present width

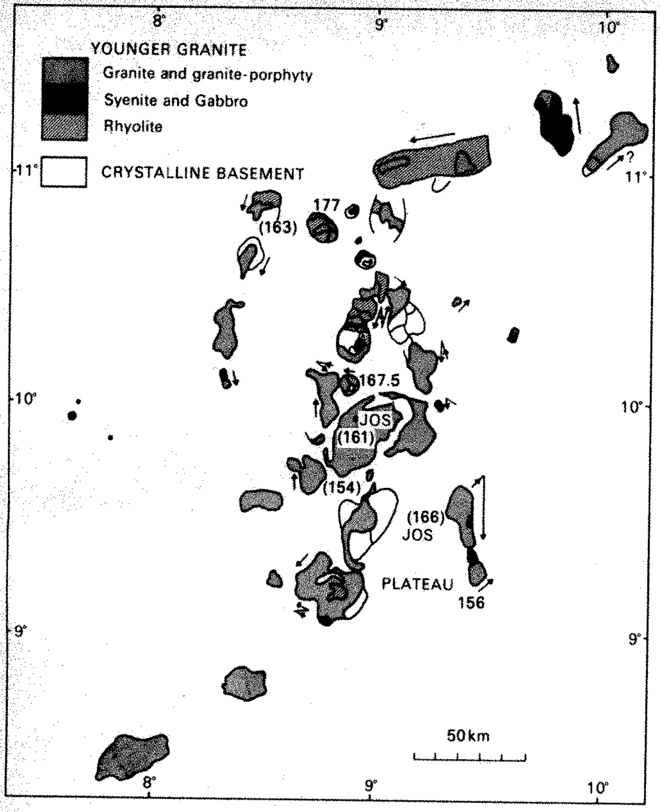

Fig. 2 Complexes of the Nigerian Younger Granite province, with age data determined by van Breemen and Bowden and by Jacobsen *et al.* (ref. 27—numbers in brackets). →, Migration of centres within complexes, taken from geological relationships established in ref. 8. There are frequent reversals of trend. There are no arrows in the central part of the Jos Plateau because the intrusions are of irregular shape and display very complex relationships. Paucity of arrows in peripheral regions is due to lack of published geological information.

by mid-Cretaceous times, the age of the youngest White Mountain intrusives—in other words the plume should by then have been beneath a point more than 1,000 km offshore.

Whatever the nature of the thermal high that gave rise to the White Mountain intrusions, it must have remained beneath New Hampshire and moved with the North American plate throughout its active life.

(2) The Jurassic Younger Granite complexes of Nigeria have been linked with Ascension Island as the products of a similar plume, that remained fixed as the African plate moved northeastward over it, during opening of the South Atlantic[4,7]. Figure 2 summarizes available radiometric ages[7,27] as well as directions of migration within individual complexes, determined from published geological maps and descriptions[8].

Here again there is no consistent pattern, either in the age distribution between complexes or in the migration of centres within them, that could be taken as evidence for regarding these granites as the products of a single stationary mantle plume. Nor is there any geological evidence for linking such a plume with Ascension Island—which incidentally lies west of the Mid-Atlantic ridge, on the opposite side of the spreading axis from West Africa.

On the other hand, there is abundant geological evidence that the Nigerian Cretaceous was characterized by considerable magmatism just south of the Younger Granite province, in the Benue trough, which developed as South America and Africa finally separated around 100 m.y. ago[9,10]. (In this connexion note the recent convincing demonstration[11] that there cannot have been any Cretaceous seafloor spreading, let alone subduction, beneath the Benue trough.) In Tertiary to Recent times widespread continental alkaline basaltic and related magmatism developed not only over the site of the Younger Granite province and in the Benue trough itself, but also in adjacent Cameroun[12,13], where granitic complexes of Lower Tertiary age, petrologically similar to the Nigerian Younger granites, are also known[28]. This Gulf of Guinea magmatic province has been intermittently active from Jurassic times to the present, and is well known as one of Africa's major crustal swells[14,15].

In both these examples, it is evident that broad thermal highs, or megaplumes, with horizontal dimensions measurable in hundreds of km, lay beneath the crust and remained active over long periods, ~100 to 200 m.y. These megaplumes moved with the lithosphere, changing shape and position to a limited extent, but in ways not obviously related to plate movements.

Local hotter spots developed within these megaplumes, generating columns of magma up to about 10 km across, very much resembling the "asthenoliths" of Beloussov[29]. These columns formed the individual centres in the White Mountain and Jos Plateau provinces.

The basic misconception informing hypotheses such as that of Rhodes[4] has been first to identify each of these centres as the product of the same small stationary plume and then to use the shifting positions of those centres to chart motions of the lithosphere over the plume. In fact the distribution of activity of these small local plumes is much more likely to be controlled principally by deep lineament systems[12,16,17,19], which probably also control the pattern of continental break-up[18] and the positions of some transform faults in oceanic crust[30].

An excellent example of the distinction that must be made between the broad megaplume that underlies an extensive magmatic province and the narrow local columns (or plumes or asthenoliths) of active magma that rise from it into the crust, can be found in Iceland, where Schilling[20] has demonstrated that a relatively narrow and elongate megaplume underlies the central volcanic belt. Local hotter spots within the megaplume are responsible for individual volcanic outbreaks which occur unpredictably at various points along the belt, showing no discernible pattern of migration (Askja, 1961; Surtsey, 1963; Hekla, 1970; Heimaey, 1972).

The Icelandic megaplume is unquestionably one that has remained stationary with respect to moving lithosphere for at least 15 m.y., and possibly more. Further, the Hawaiian chain seems to be the product of a single rather small plume, without an associated megaplume—and the evidence is that it too has remained stationary in relation to the lithosphere. But the New Hampshire and Nigerian granite provinces as well as the Mesozoic province in southwestern Africa cited by Kröner[16] are equally convincing examples of megaplumes that moved long distances with the overlying lithosphere.

What are the reasons for this contrasted behaviour? Differences in the inferred shape and size and in the associated magmatism provide an obvious clue. The plume beneath Hawaii must have the form of a narrow column[3], not much wider than the individual volcanoes to which it has given rise, and the predominant magma type is tholeiitic basalt. The central volcanic belt of Iceland is evidently underlain by a rather steep-sided tabular megaplume[20], and the principal magmatic product is again tholeiitic basalt. The megaplumes beneath New Hampshire and Nigeria were broader and shallower, for salic magmas are by far the most abundant variety, implying a lower degree of partial melting in the upper mantle, than is required to generate basaltic magma. So the relatively hot and sharply profiled Hawaiian plume can remain stationary and pierce the moving oceanic lithosphere above it, leaving a plume trace in the form of an island chain. In the same way, the Icelandic megaplume can continue to split the lithosphere above it and contribute to seafloor spreading in the North Atlantic. By contrast, the broad, shallow and relatively cool "salic" megaplumes achieve much less penetration of the lithosphere; in consequence they tend to remain beneath the continental swells, rather like air bubbles trapped below the gentle undulations of an ice floe. They cannot remain stationary, but must move with the lithosphere.

The trapped bubble analogy can help to illuminate the "chicken and egg" problem of whether continental swells are the cause or result of the underlying megaplumes responsible for their associated magmatism. Bailey suggests[21] that the swells control the magmatism, and they may result from lateral stresses set up by plate interactions[9,22], a proposition for which there is some evidence[31]. Gentle buckling of the continental lithosphere could lead to pressure release and partial melting in the deep crust or underlying mantle, an optimum setting for generation of salic magmatism[21].

The air bubbles beneath an ice floe will change shape and position in response to changes in the pattern of overlying undulations. If changes in lateral tectonic stresses with time cause changes in the pattern of continental lithosphere swells, then the broad megaplumes beneath them will change in shape and position also. For example, the immense Karroo magmatic province of South Africa, Rhodesia and Mozambique was active throughout much of Triassic and Jurassic time. The long period and diverse pattern of volcanic and intrusive activity[23] suggest that this region was underlain by a large and complex megaplume system of considerable longevity. It is tempting to suggest that in Cretaceous times this megaplume migrated northward in response to stresses set up during the breakup of Gondwanaland, and became responsible for the extensive salic magmatism of southern Malawi[24]. In the same way, the giant Kenya–Ethiopean volcanic province[25,26] is likely to have been underlain since Lower Tertiary times, by another megaplume which has changed its shape and position, perhaps in response to stresses accompanying collision of the African and Eurasian plates.

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Dingle's Question

IT would be profitless to deal separately with the latest "answers"[1–5] to my question; their diversity tells its own tale, and the writers may see their misjudgments corrected in my book[6]. I have through the years put the question in various forms to meet successive obscurations, but in vain. Though wholly understandable to any ordinary layman it is at once submerged in such mathematical and metaphysical mysticism that normal readers either conclude that its simplicity must be deceptive and I deluded, or express to me their astonishment at the denseness of the "authorities". I try once more to free the stark simplicity of the matter from alien technicalities.

The "situation" is just that two exactly similar clocks, A and B, are in uniform relative motion. Then: (1) the special relativity theory says that they work at different rates, that is, one works manifestly faster than the other; (2) because they differ only in velocity the rate-difference must be directly connected with the velocity-difference, that is, the faster *working* clock must be the faster (or slower) *moving* clock; (3) the theory allows physical meaning only to *relative* velocity, so any supposed *individual* velocities of A and B can be interchanged without affecting anything observable; (4) it therefore follows from (2) that the rates of *working* are interchangeable; (5) because this would require the impossibility that A worked observably faster and slower than B, the question arises—how does the theory decide which it must do?

That is all. Every word has its ordinary meaning, there is no appeal to mathematics (all the mathematics involved is used up in deriving (1) from the postulates of the theory and is not in dispute) or to metaphysics ("time dilation", time turning into space, and so on) or to observers (every statement is objective and holds good for everyone who observes, or does not observe, anything) or to coordinate systems or frames of reference, except in the trivial sense that the phrase "supposed *individual* velocities of A and B" could, but need not, be expressed technically as "chosen coordinate system". This suffices to show that the "answers" of Jacob[3], Whippman[4] and Stedman[5], which all depend on these irrelevancies, are simply smokescreens.

The only item in the above statement which is ever challenged (almost always indirectly) is (1). The words "rate", "faster", and so on have been give esoteric meanings to make the obvious inscrutable, notwithstanding that for fifty years no one mistook their plain sense. Clearly, because words can be defined only by using other words which can themselves be challenged, this process could be endless, and a direct appeal to Einstein's writings is impossible because his words were German. I will, however, present two considerations which I think might make it difficult for anyone to challenge the layman's understanding of (1) without a blush.

Einstein made the following statement[7]: "If at the points P and Q" (Einstein wrote A and B, but I have used these letters otherwise) "of [the 'stationary' system] there are stationary clocks which, viewed in the stationary system, are synchronous; and if the clock at P is moved with the velocity v along the line PQ to Q, then on its arrival at Q the two clocks no longer synchronize, but the clock moved from P to Q lags behind the other which has remained at Q by" a precise amount. Here both the initial synchronization and final comparison can be made objectively by photography; the theory defines the former wholly in terms of the readings of clocks when a beam of light strikes them, which are clearly the same however the observer of the readings moves, and the latter is made when the clocks coincide. Further, I think no one (except Fremlin[2]) can doubt that if Einstein had attached importance to the acceleration that changes the relative velocity from O to v, he would not have made the literally absurd statement that the velocity was v throughout, and given a precise value for the "lag" which holds only if the acceleration is ineffective. Hence it is inescapable that, during the motion, one clock has, according to the theory, actually recorded a smaller interval than the other, and has therefore worked at a slower rate, which suffices to confirm (1). It also follows that (unless, indeed, nature has uniquely named each point of space) each clock has performed that feat.

Second, I consider the "twin paradox" situation, because two correspondents have dragged it in though I have repeatedly stressed that my argument is independent of it. In a recent example Paul travels at birth to a distant planet and returns 3 d old to find his earth-bound twin Peter 30 yr old. I consider only the outward journey at constant velocity up to the start of the reversing process (Paul's initial acceleration is negligible, as before, and in this case could be proved so if space allowed). My critics and I accept that because for each twin the outward and return journeys take the same time, the theory requires Paul to reach the planet 1.5 d old when Peter is 15 yr old. (It also requires these ages to be reversed, but I ignore that here, for, to establish my item (1), I keep to what is agreed). If, therefore, Paul and Peter have only apparently aged at different rates, and Paul really arrives aged 15 yr, his reversal and return must restore him from teenage to babyhood. This has not yet been explicitly claimed in defence of relativistic asymmetrical ageing (though it has implicitly), and I venture to assume that the reader will accept its impossibility as a proof that (1) is a true statement. The other items then, I think, need no defence, so the question in (5) remains unanswered.

But I must again point to the really tragic (it is not too strong a word) aspect of this matter which the infinite variety of the "answers" to my question places beyond doubt, namely, that it has become impossible for mathematical physicists to believe that this theory can be wrong. As Armstrong pertinently suggests[1], if there is an answer to my very simple question, those who understand the theory would be expected to agree on what it is. Instead, one esoteric evasion after another (the new "answers" are, of course, only the tip of a many-splendoured iceberg) is served up by those who consistently ignore their predecessors and agree only in their insistence that I must be wrong. It is now easier for a camel to pass through a needle's eye than for a mathematical physicist to conceive that whatever is possible for his symbols is not of necessity possible for physical bodies. No state of mind can, in present circumstances (or, morally, in any circumstances) be more ominous than that which this controversy has shown to be practically universal among these practitioners. Once more I beg those—be they physicists, biologists, or public men of any description—in whose power it lies, to read the unmistakable signs of the times and take such steps as will ensure that in science the traditional absolute authority of reason and experience over automatic adherence to any theory, however attractive and temporarily successful, is restored before the inevitable consequences of neglecting that duty come upon us.

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BIOLOGICAL SCIENCES

Tissue-specific Sorting-out in Two Dimensions in Relation to Contact Inhibition of Cell Movement

IT is thought that the monolayering of cells which takes place on a substratum in tissue culture results from "contact inhibition of cell movement", that is inhibition of the movement of a cell in the direction of contact with another[1]. If it is the movement of a cell toward a contacted neighbour that is inhibited, cells which are surrounded on all sides by other cells should be immobilized[2]. Yet cells in heterotypic aggregates must and do move in the course of tissue-specific sorting out, even though they are surrounded in all directions by other cells[3,4]. Because of this we wondered whether "contact inhibition of movement" requires a solid substratum. We decided to see whether cells of different tissue origin combined in a mixed monolayer would be immobilized and prevented from sorting-out.

Four-day-old limb bud mesenchyme and 7-d-old liver from chick embryos were dissociated in 0.1% crude trypsin in calcium- and magnesium-free Hanks' solution[5]. The dissociated cells were mixed in minimum essential medium plus 10% horse serum and the suspension put into 35-mm tissue culture dishes so that there were just enough cells (8×10^6) to cover the dish bottom completely after spreading. The dishes were incubated at 37° C in a water-saturated atmosphere containing 5% CO_2

Examination of cultures after 48 h showed (*a*) that the monolayer was confluent and (*b*) that sorting-out had occurred. The liver cells had collected into rounded islands within a continuous phase of limb bud cells (Fig. 1). (The significance of this particular configuration will be discussed elsewhere.) Subsequent observations showed that confluency was achieved in such cultures after 10–20 h. The crucial question was whether sorting-out continued after confluency. Time-lapse cinematography and cell counting on fixed and stained monolayers showed that sorting-out began soon after the cultures had been set up, but that liver groups continued to increase in size and decrease in number after confluency was attained (at least up to 48 h). Furthermore, all cells remained in monolayer: cells did not pass over or under one another.

These findings are of interest for two reasons. First, the demonstration that cell sorting can occur in two dimensions opens up the possibility of directly observing the behaviour of sorting cells which until now has occurred obscurely in the interior of three-dimensional aggregates. Second, our results suggest that inhibition of cell locomotion is not a necessary part of the cause of monolayering. This is because the cells in our cultures were clearly able to continue sorting movements while experiencing contact inhibition (inhibition of

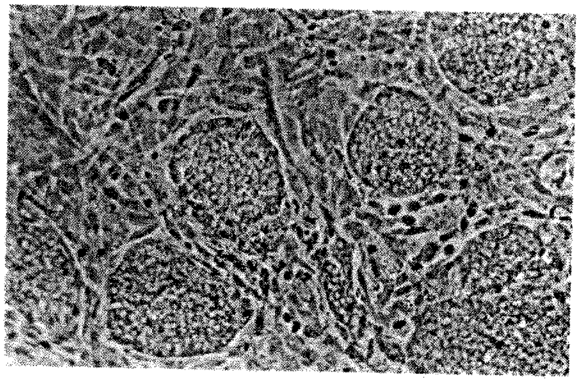

Fig. 1 Monolayer culture (48 h) of chick embryo liver and limb bud cells showing rounded liver islands within a continuous phase of limb bud (×200).

overlapping) on all sides within a confluent monolayer. The films also showed that many cells exhibited both ruffling activity and movement while apparently totally and closely surrounded by other cells.

We suggest that the concept of "contact inhibition of cell movement" requires re-examination, in the sense that monolayers, developing as cells cease their forward motion upon collision with other cells, may result primarily not from an inhibition of cell movement *per se* but rather from a direct discouragement of overlapping, perhaps due to adhesive phenomena[6,7].

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Hapten-specific Helper Effects in Antibody Formation

ANTIBODY synthesis is known to result from cooperation between antigen specific bursal equivalent (B) cells and thymus-dependent (T) cells[1,2]. When hapten-protein conjugates are used as antigens, the T cells recognize the carrier protein determinants and the B cells produce the hapten-specific antibody[3,4].

Since our original demonstration *in vivo* of hapten-specific delayed hypersensitivity to the azobenzenearsonate (ABA) group[5], others have shown that this reaction also possesses many of the *in vitro* attributes of a T cell-mediated cellular response[6-8], and may function as a helper in cooperating with B cells to produce antibody[9].

Here, we present further evidence for the ability of ABA-specific sensitivity to perform a helper function and some additional requirements for successful collaboration between ABA-specific T cells and dinitrophenol-specific (DNP-specific) antibody producing B cells.

Polymers of L-glutamic-L-alanine-L-tyrosine (L-GAT) and D-glutamic-D-alanine-D-tyrosine (D-GAT) were coupled with DNP mustard (DNPmust) groups by the reaction of free COOH groups with a DNP-nitrogen mustard and having the structure $DNP\text{-}N\text{-}(CH_2)_3S\text{-}(CH_2)_2Cl$. Both D- and L-polymers were found to contain approximately 3.3×10^{-7} mol DNP mg^{-1} polymer by spectrophotometric analysis.

Conjugation with ABA groups was achieved by addition of ABA-diazoniumfluoborate salt to the DNPmust-polymer at *p*H 8.0. ABA content, assayed by spectrophotometric analysis, was found to be approximately 0.8×10^{-7} mol ABA mg^{-1} polymer.

Skin tests with the double hapten conjugate of the L-polymer were positive in guinea-pigs immunized with ABA-N-acetyl-tyrosine in complete Freund's adjuvant (CFA), demonstrating that recognition of the ABA group was not blocked by addition of DNPmust groups. As previously reported[10], skin tests with either single or double hapten conjugates of the D-polymer were negative.

Helper function was studied in three groups of seven white male guinea-pigs (350 g). The first two groups received 2×10^{-7} mol ABA-Tyr in CFA in four foot pads to produce hapten-specific delayed sensitivity, and 10 μg of the DNPmust conjugate of bovine serum albumin (DNPmust-BSA) in CFA intraperitoneally to prime for antibody formation. The third group received CFA alone in the four foot pads and DNPmust-BSA in CFA intraperitoneally.

All animals were bled at intervals and sera were assayed for γ_2 anti-DNP antibody by the passive haemolytic technique[11], using tanned sheep red cells coated with DNP-human γ-globulin (DNP-HGG). After 6 weeks, anti-DNP titres had declined to low levels and the animals were ready for booster injections. Group 1 was given 0.5 mg ABA-DNPmust-D-GAT, half intradermally at two sites and the rest intraperitoneally. Groups 2 and 3 were given the same dose of the ABA-DNPmust-L-GAT conjugate. Skin sites were examined after 3 and 24 h.

Virtually all animals exhibited moderate Arthus reactions after 3 h, consisting of about 10 to 15 mm of oedema with some haemorrhage. This was attributable to the reaction of circulating anti-DNP antibody with DNPmust-haptens on both D- and L-polymers. By 24 h all Arthus reactions had subsided to be replaced only in Group 2 animals by delayed reactions of approximately 20 mm induration and erythema, that is, delayed reactions were produced only in the ABA-sensitized animals given ABA-DNPmust-L-polymer.

Table 1 Anti-DNP Antibody Production in Guinea-pigs Following Booster Injection of ABA-DNPmust-L and D-GAT

Group	Treatment	Boosted with	Average anti-DNP titre Pre-boost	Average anti-DNP titre Post-boost
1	ABA-Tyr in CFA DNP-BSA in CFA	ABA-DNPmust-D-GAT	63	80
2	ABA-Tyr in CFA DNP-BSA in CFA	ABA-DNPmust-L-GAT	71	968
3	Saline in CFA DNP-BSA in CFA	ABA-DNPmust-L-GAT	38	48

One week after the booster injection, the animals were bled and the pre- and post-booster sera assayed for γ_2 anti-DNP antibody by passive haemolysis. From the results in Table 1, it may be seen that guinea-pigs in which only B cell priming for DNP antibody production was performed (Group 3) did not show a significant boost in anti-DNP production when given the double hapten conjugate of L-GAT. The animals primed for both ABA helper cells and DNP antibody producing cells showed a marked increase in anti-DNP production following boosting with the double hapten conjugate of L-GAT (Group 2).

These results confirm that ABA sensitivity can serve as a helper function in enhancing antibody formation to the DNP hapten in suitably primed animals. In the absence of ABA sensitivity, no booster effect is obtained as the DNP moiety is recognized by the animal on two different carriers for priming and boosting and the rules of carrier specificity for an anamnestic response are in force[12].

One possible reason for the different behaviour of the two polymers is that the DNP and ABA portions of the D- and L-polymers are not equally sterically accessible to the receptors on B or T cells.

Although accessibility of DNP groups to receptors on the potential antibody-producing B cells was not directly tested, it could be seen that animals exhibited anti-DNP antibody-mediated Arthus reactions of identical severity with conjugates of D- or L-polymers. Moreover, in an *in vitro* test, tanned sheep red cells coated with ABA-DNPmust-L-GAT or ABA-

DNPmust-D-GAT gave equal haemolytic titres when assayed with guinea-pig sera produced against DNP-BSA Thus, the DNP groups on the D- and L-polymers were similarly accessible to the products of B cells, if not their receptors

Table 2 Inhibition by ABA-D-GAT of Stimulation *in vitro* of Lymphocytes from ABA-sensitive Guinea-pigs

Stimulating antigen	Inhibitor	Added at time	Stimulation index
Control	0	0	1 0
ABA-Tyr (100 μg)	0	0	9 9
ABA-Tyr (100 μg)	ABA-poly-D-GAT (25 μg)	−4 h	4 7
ABA-Tyr (100 μg)	ABA-poly-D-GAT (25 μg)	+4 h	7 8
None	ABA-poly-D-GAT (100 μg)	0	0 8

Recognition of ABA groups by receptors on T cells is more difficult to determine We have long known that only ABA on L-polymers actively elicits all the *in vivo* or *in vitro* manifestations of cell mediated immunity The failure of ABA conjugates of D-polymers to function cannot be attributed solely to structural features of the D-tyrosine to which the ABA group is attached, as an ABA-conjugate of D-tyrosine in an otherwise all L-amino acid polymer gives good reactions[13]

To find out if ABA groups on the D-polymer can be "seen" by T cells, the possible competitive inhibition of stimulation of ABA sensitive T cells was studied Lymph node cells from guinea-pigs sensitized with ABA-Tyr in CFA were cultured with the antigen ABA-Tyr and stimulation detected by uptake of ^{3}H-thymidine The results of one such experiment in which varied amounts of ABA-D-GAT were added 4 h before or 4 h after the stimulating dose of ABA-Tyr are shown in Table 2 While 100 μg of ABA-Tyr alone gave a stimulation index (SI) of 9 9, addition of as little as 25 μg ABA-D-GAT gave a reduction of the SI to 4 7 when given 4 h before Addition 4 h after stimulation had much less effect (SI = 7 8)

Thus, the ABA groups on the L-polymer can be considered to be "seen" by receptors on T lymphocytes, as judged by reactivity, whereas the ABA groups on the D-polymer can only be inferred to combine with the same receptors as measured by inhibitive activity

The failure of the ABA-DNPmust-D-GAT polymer to produce sufficient cooperation for antibody production could be resolved by assuming that mere physical coupling of T and B cells through the binding of their receptors to suitable determinants is not a sufficient condition for antibody formation Other studies have indicated that T cells must be activated to synthesize RNA and protein before they can initiate antibody production by B cells[14] As the ABA on D-polymers cannot activate the T cell, it cannot lead to cooperative antibody production One possible reason for this may be a requirement for some sort of preliminary processing of antigen by macrophages before T cells are activated Some recent studies[15,16] have suggested that this may not occur with D-amino acid polymers

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ON page 43 of the issue of July 6, 1973 we published a Letter by Dr Ernest B Hook and Dr William J Schull In the course of sub-editing, the Letter was amended by us, but due to delays in the post the authors were unable to point out before publication that the sense of the Letter had been altered in two places A correct version of the Letter is printed below

The authors have also taken this opportunity to correct certain of the data in the tables which appeared in the original version

Why is the XX Fitter? Evidence Consistent with an Effect of X-heterosis in the Human Female from Sex Ratio Data in Offspring of First Cousin Marriages

ALTHOUGH the human female is known to be more viable, on the average, than the human male, the biological mechanisms for this difference are poorly understood A relevant question is, to what extent does heterozygosity for X-linked loci contribute to survival of the XX female? The advantage accruing to the XX female because of this factor may be defined as X-heterosis[1] Most instances of serious X-linked disorders such as haemophilia occur in males, but the total incidence of such severe diseases is relatively small and cannot account for the observed sex differences in age specific mortality rates It is conceivable that X-heterosis is relatively insignificant in the total population, and that the bulk of the observed sex difference is attributable to physiological factors that are a consequence of sex differentiation (for example, the apparent oestrogen-sparing effect on coronary heart disease) and/or to psycho-cultural factors that may pertain to diminished exposure of woman to environmental hazards (for example, industrial pollutants)

Large sex differences in foetal death rates are not as well established as sex differences in postnatal death rates But even if the rates of foetal loss of males and females were identical, a significant X-heterotic effect could exist in XX foetuses but be balanced by relatively beneficial physiological factors affecting primarily male foetuses

Moreover, X-heterozygosity may not necessarily be beneficial Evidence suggests that heterozygosity at the Xg^a blood group locus in one population at least has a deleterious effect during gestation because of a dearth of heterozygous female foetuses of Xg^a negative mothers[2] As yet, no evidence for a large beneficial effect of X-heterozygosity in any population for

Table 1 Livebirths, Foetal Loss and Death, by Marriage Subset*

		Number of families		Livebirths		Stillbirths			Abortions		Accidental deaths		Natural deaths		Deaths of unknown cause		Twin sets	
		Total	Fertile	M	F	M	F	?	Nat	Th	M	F	M	F	M	F	M	F
X-Outbred Type 1	Rural koseki	96	92	232½†	275	2½†	0	2	11	1	12	2	49	52	3	8	1‡	2
	Rural non-koseki	18	12	21	24	1	1	0	0	0	0	0	6	7	0	1	0	0
	Urban non-koseki	13	13	22	26	0	0	0	3	5	0	0	3	6	0	0	0	0
	Totals	127	117	275½†	325	3½†	1	2	14	6	12	2	58	65	3	9	1	2
X-Outbred Type 2	Rural koseki	113	107	255	273	3	3	5	8	16	6	0	61	49	0	1	1	2§
	Rural non-koseki	14	8	15	12	1	0	0	0	0	0	0	4	1	0	0	0	0
	Urban non-koseki	3	2	2	1	0	0	0	0	0	1	0	1	0	0	0	0	0
	Totals	130	117	272	286	4	3	5	8	16	7	0	66	50	0	1	1	2
X-Inbred Type 3	Rural koseki	111	104	290	258	6	2	2	5	3	8	2	63½†	58	8	5	1	1
	Rural non-koseki	12	9	19	20	0	0	0	1	0	0	0	8	6	0	1	0	0
	Urban non-koseki	14	12	22	20	0	0	1	1	0	0	0	3	0	1	1	0	0
	Totals	137	125	331	298	6	2	3	7	3	8	2	74½†	64	9	7	1	1
X-Inbred Type 4	Rural koseki	143	129	340	330	6	3	2	17	6	7	0	71	69½†	2	0	1	1
	Rural non-koseki	19	15	41	21	0	0	2	1	3	3	0	10	10	0	0	0	0
	Urban non-koseki	9	7	24	12	0	1	0	0	2	1	0	4	1	0	0	0	0
	Totals	171	151	405	363	6	4	4	18	11	11	0	85	80½†	2	0	1	1
X-Inbred all	Totals	308	276	736	661	12	6	7	25	14	19	2	159½†	144½†	11	7	2	2
X-Outbred all	Totals	257	234	547½†	611	7½†	4	7	22	22	19	2	124	115	3	10	2	4

* Pedigree and other data were collected in 1964 through a census directed at all marriages, legal or consensual, represented by at least one spouse alive and residing in Hirado at the time of the census[5-7] Some 10,530 unions contracted subsequent to 1890 were ascertained, and their reproductive histories recorded The information obtained at interview was routinely compared with the existing records of the public health office, the agricultural and fishing cooperatives, the tax office, and the kosekika, the office of custody of the koseki, the household censuses required by law in Japan[8] All vital events which affect the composition of a family such as marriages, births and deaths must be reported to this office Where there was a discrepancy between the interview and the koseki, the data from the latter were generally used As reporting of livebirths is very complete whereas most abortions and many stillbirths go unrecorded, the observations here reported on abortions and stillbirths stem almost exclusively from interviews, whereas the livebirth data are a synthesis of interviews and koseki observations and are much more complete Information on type of death was that obtained by interview Most of the natural deaths were in early childhood years About 20% of the deaths recorded were to those over 21 yr of age Deaths of unknown cause were those which were recorded in the koseki but not recalled by those being interviewed Almost all the deaths in this category were of individuals who had died in infancy All twin pairs were concordant for sex, and in view of the very low rate of dizygotic twinning in Japan, each such set of twins was scored as one birth of that sex One set of triplets resulted in two stillborn females and one liveborn male and was scored as one male livebirth and one female stillbirth (Type 2-Outbred) The following abbreviations are used M, male; F, female, Nat, natural abortion, Th, therapeutic abortion There was one child of unknown sex in the rural koseki group of Type 3 inbred marriage, and one natural death to a child of unspecified sex in the rural non-koseki group of Type 4 inbred marriage

† Where one of the twins was liveborn, the other stillborn or only one died, the entry "½" is made in appropriate column (see above for rationale) ‡ This twin pair included one liveborn and one stillborn § Both members of one twin set were stillborn

any trait has been presented, and there are no published data available for an analysis of the net total effect of X-heterosis on differential survival in any population

We present here data which suggest that, among the population of the Japanese Island of Hirado, X-heterosis contributed quite considerably to female survival during gestation There is also a trend consistent with an X-heterotic effect on postnatal survival

The theoretical basis for the approach used has been described in detail[1] and the discussion is limited here to first cousin offspring (see Fig 1) Briefly, of the four types of first cousin marriages, two, types 1 and 2, may be said to be "X-outbred" as they result in XX daughters who are X-outbred and two, types 3 and 4, "X-inbred" as they result in XX daughters who are X-inbred If X-heterosis is significant during gestation then a higher sex ratio at birth (that is of males to females) would be expected in the infants of X-inbred subsets of first cousin marriages than in those of the X-outbred subsets And if X-heterosis is significant postnatally then X-outbred females should be relatively protected by this effect compared with X-inbred females The rationale for these considerations is presented in Fig 1

The data presented here were obtained from a large investigation of consanguineous marriages on the island of Hirado (Table 1) There were 565 unions of first cousins for which data were available, this was the largest category of consanguineous matings encountered and the only one on which a detailed analysis was undertaken The sex ratios of livebirths, stillbirths, and postnatal deaths by first cousin subset appear in Table 1 along with details on the ascertainment and classification of the data

The secondary sex ratios in both X-inbred subsets are higher than in both X-outbred subsets (Table 2) and the difference between the sex ratios of X-inbred subsets and X-outbred subsets is statistically significant (547 5/611 =0 896 against 736/661 =1 113, chi^2=7 24, $df=1$, $P<0\ 01$) If attention is restricted to the most homogenous groups within a subset, the rural, koseki checked pedigrees, the same effect is present (487 5/548 against 630/588, chi^2=4 65, $df=1$, $P<0\ 05$) The differences are thus consistent with a negative effect of X-

Table 2 Livebirth Sex Ratio and Death Rates by Cousin Subset

	Livebirth sex ratio	Non-accidental death rate* Male	Non-accidental death rate* Female
X-Outbred			
Type 1	0.848	0.221	0.228
Type 2	0.951	0.243	0.178
All	0.896	0.232	0.205
X-Inbred			
Type 3	1.111	0.252	0.238
Type 4	1.116	0.215	0.222
All	1.113	0.232	0.229

*The non-accidental death rate is the sum of the natural deaths and deaths of "unknown cause" (which were almost all in the infant years) divided by the number of livebirths.

Table 3 Socioeconomic Status and Maternal Age at Birth of First Child by First Cousin Subset

	Socioeconomic status* Mean	Socioeconomic status* Variance	Maternal age at birth of first child (years) Mean	Maternal age at birth of first child (years) Variance
X-Outbred				
Type 1	16.73	36.33	21.60	8.38
Type 2	18.28	86.98	22.22	11.61
X-Inbred				
Type 3	16.82	39.43	21.61	15.46
Type 4	17.36	71.43	21.92	13.82

* Socioeconomic status is represented here by a score which is the sum of the coded values associated with parental occupation, education, and related variables. See ref. 7 for details.

Table 4 Distribution of Families by Decade of Marriage

	–1899	1900–1909	1910–1919	1920–1929	1930–1939	1940–1949	1950–1959	1960–
X-Outbred Type 1 (127)	2.4%	8.7%	13.4%	18.1%	10.2%	30.0%	14.2%	3.1%
X-Outbred Type 2 (130)	0.8%	3.8%	14.6%	17.0%	13.8%	28.5%	16.9%	4.6%
Total X-Outbred (257)	1.6%	6.2%	14.0%	17.5%	12.1%	29.2%	15.6%	3.9%
X-Inbred type 3 (136)*	1.5%	8.1%	14.0%	22.8%	13.2%	26.5%	11.8%	2.2%
X-Inbred Type 4 (171)	2.9%	2.9%	18.7%	17.5%	16.4%	26.3%	14.6%	0.6%
Total X-inbred (307)	2.3%	5.2%	16.6%	19.9%	15.0%	26.4%	13.4%	1.3%

* In one family the date of marriage is not available.

inbreeding during gestation, which leads to a net loss of females in the X-inbred subsets. There is, however, no striking difference in foetal loss between X-inbred and X-outbred subsets. Although even late foetal wastage was probably very poorly ascertained, the lack of any difference here suggests that if X-heterozygosity is responsible for the sex ratio difference at birth, females lost because of X-inbreeding may be lost early in gestation, perhaps before awareness of pregnancy, and reproductive compensation readily occurs in view of the lack of any significant effect on total fertility.

The apparent magnitude of the effect is relatively large, and it may be specific to the population under investigation. In addition, it is present in spite of any influence polymorphism at the *Xg^a^* locus might have had on sex ratio in those studied, but we have no data on the frequency of such alleles at this locus on the Island. Furthermore, the observed sex-ratio in the X-outbred group is not necessarily what would be predicted in a completely outbred control population, as sex differential responses to autosomal inbreeding in both X-inbred and X-outbred subsets may also have had an effect on the sex ratios in those studied here.

Another trend of interest is the postnatal death rate. If X-heterosis is significant for postnatal survival then X-inbred females should have greater mortality and morbidity than X-outbred females, but there should be no effect in the males. What data are available are consistent with this hypothesis. Although deaths have probably been poorly ascertained because of migration and other factors, most of those recorded represent deaths in infancy and early childhood. The mortality rates for non-accidental deaths (as defined in Table 2) in males in the two groups are identical, 0.232. But the recorded death rate in X-inbred females, 0.229, is about 12% greater than that in X-outbred females, 0.205. With the number of individuals involved, however, the trend is not yet significant at the 5% level.

Most studies to date of offspring of consanguineous unions have compared them with outbred individuals, and conclusions may always be vitiated by possible systematic differences between the related and unrelated families. Our study, by making comparisons within the inbred group of first cousin offspring, avoids many of these pitfalls. It is still possible, however, that some systematic differences between the subsets might have contributed to the differences in sex ratios. Comparisons of X-inbred groups and X-outbred groups with regard to a number of possibly relevant factors are presented in Tables 3–6. There appear to be no major differences with regard to decade of marriage, geographical distribution on the island,

Table 5 Distribution of Families by Religion

	Buddhist	Catholic	Kakure*	Other
X-Outbred – 1 (127)	81.1%	0.8%	17.3%	0.8%
X-Outbred – 2 (130)	80.0%	0%	16.2%	3.8%
X-Outbred total (257)	80.5%	0.4%	16.7%	2.3%
X-Inbred – 3 (135)	79.3%	1.5%	17.0%	2.2%
X-Inbred – 4 (170)	83.5%	0.6%	12.4%	3.5%
X-Inbred total (305)†	81.6%	1.0%	14.3%	3.0%

* A syncretic cult incorporating elements of Buddhism and Catholicism.

† 2 intermarriages are excluded, and data are not available on one family.

Table 6 Distribution of Families by Geographic Area

	Hirado – 1	Hirado – 2	Nakano	Himosashi	Shishi	Nakatsura	Tsuyoshi	Shijiki
X-Outbred Type 1 (127)	9.4%	25.2%	13.4%	10.2%	20.5%	7.1%	6.3%	7.9%
X-Outbred Type 2 (130)	9.2%	17.7%	9.2%	22.3%	18.5%	10.0%	7.7%	5.4%
Total X-outbred (257)	9.3%	21.4%	11.3%	16.3%	19.5%	8.6%	7.0%	6.6%
X-Inbred Type 3 (137)	10.9%	22.6%	15.3%	12.4%	16.1%	3.6%	8.0%	10.9%
X-Inbred Type 4 (171)	9.9%	17.5%	7.6%	18.1%	15.1%	7.0%	12.3%	12.3%
Total X-inbred (308)	10.4%	19.8%	11.0%	15.6%	15.6%	5.5%	10.4%	11.7%

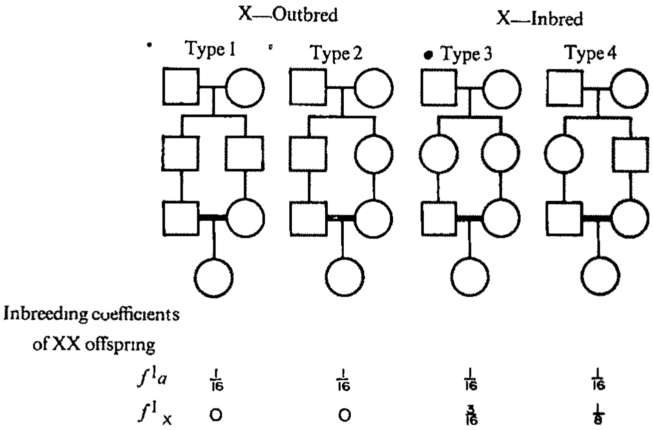
X—Outbred
X—Inbred
Type 1
Type 2
Type 3
Type 4
Inbreeding coefficients of XX offspring
f^1a 1/16 1/16 1/16 1/16
$f^1{}_x$ 0 0 3/16 1/8

Fig. 1 Possible pedigrees of XX offspring of first cousin marriages Note that XXs born to first cousins have identical autosomal inbreeding coefficients but may have different X chromosome inbreeding coefficients depending on the parental relationship If heterozygosity for X-linked loci has an effect on a particular attribute, say, survival, this effect should be less for X-inbred females (that is, those for whom $f^1{}_x > 0$) who will be more homozygous for X-linked loci, on the average, than females for whom $f^1{}_x = 0$, that is, X-outbred females If X-heterozygosity is beneficial, this advantage attributable to outbreeding should by definition be more significant for X-outbred than X-inbred females but would have no effect on XY males Therefore, if X-heterozygosity contributes positively to survival to age *n*, the sex ratios (M/F) of X-outbred groups (that is, those in which X-outbred females occur, types 1 and 2 above) should be less than those of the X-inbred groups (those in which X-inbred females occur, types 3 and 4) and conversely if there is a negative effect The secondary sex ratios, that is those noted at birth, should reflect the net effect of X-heterozygosity during gestation The occurrence of XO females and males with more than one X-chromosome will confound the theoretical expectation, but the instances of such individuals in all populations studied to date appear to be less than 0 2% and are thus likely to be of trivial magnitude See refs 1, 3 and 4 for further discussion

maternal age at birth of the first child, socioeconomic status, or religion This does not exclude the possibility of some other as yet unknown differences between these subsets that might be associated with altered sex ratio At present, however, the only known systematic difference between these groups is the X-inbreeding coefficients of their female members, suggesting that this is the causal factor for the sex ratio data

These observations provide, to our knowledge, the first evidence consistent with a significant deleterious effect of X-inbreeding in any mammalian population

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Test of Selection and Neutrality in Natural Populations

MORE than a century after the publication of Darwin's *Origin of Species*, the question of the relative contribution of selected and nonselected ("neutral") genetic variation to evolution is still unresolved[1,2]

A test of the theory of selective neutrality of polymorphisms has recently been suggested by Lewontin and Krakawer[3], on the basis of an idea first introduced by Cavalli-Sforza[4] in analysing human evolution The method is based on the contrasting effects of natural selection and the breeding structure on allele frequencies Whereas natural selection operates differentially on each allele, inbreeding affects all alleles similarly The inbreeding effect can be calculated in populations irrespective of their degree of isolation or their actual breeding structure, thereby avoiding manipulations with the parameters of population size, *N*, mutation rate, *u*, migration rate, *m*, and selection intensity, *s*, which are largely unknown in natural populations[3]

Spatio-temporal variation in steady state gene frequencies, in the absence of selection, reflects the breeding system alone and can estimate a parameter $\hat{F}_e$ the "effective inbreeding coefficient" across populations, or the "standardized variance of gene frequency[4]" F_e is an equilibrium value reached after many generations and involves selection and random drift The estimate is $\hat{F}_e = S^2{}_p/\bar{p}(1-\bar{p})$ where $\hat{F}_e$ is the estimate of effective inbreeding, $S^2{}_p$ is the variance in the frequency of one one of two alternative alleles across populations[3], and $\bar{p}$ is the mean frequency of the allele across populations Selectively neutral alleles will all have similar estimated $\hat{F}_e$ values in spite of their individual variation in $S^2{}_p$ and $\bar{p}$ because effective inbreeding will be identical for all genes across populations The average $\hat{F}_e$ will thus estimate the true $\hat{F}_e$ without significant heterogeneity among alleles If, however, selection is operating on some or all of the loci, their $\hat{F}_e$ values will be significantly heterogeneous and will not be estimates of the same $\hat{F}_e$ The test of homogeneity of $\hat{F}_e$ estimates from different loci in steady state is thus a test for selection The statistical properties of $\hat{F}_e$ and a sampling theory for testing heterogeneity in $\hat{F}_e$ are given in Lewontin and Krakawer[3]

Here I describe a test by the $\hat{F}_e$ method for selection and/or non-selective factors operating in natural populations of the fossorial rodent *Thomomys talpoides*, which belongs to the pocket gopher family *Geomyidae* The basic data on gene frequencies are taken from ref 5

Alloenzymatic variation in proteins encoded by 31 loci was analysed electrophoretically in 276 specimens representing eleven populations and six chromosome forms of *Thomomys talpoides* complex of pocket gophers in the southern Rockies of the USA[5] The eleven populations, their localities, abbreviations and respective diploid numbers are as follows (1) Snowy Range Pass (SR), S E Wyoming, $2n=48$, (2) Willow Creek Pass (WC), N Colorado, $2n=46$, (3) Dead Horse Creek (DH), head of White River, N Colorado, $2n=44$, Three Forks Campsite (TF), N W Colorado, $2n=40$, (5) Kaibab Plateau (KP), N Arizona, $2n=40$, (6) La Sal Mountains (LS), E Utah, $2n=60$, (7) Molas Lake (ML), S W Colorado, $2n=60$, (8) Canjilon (CN), N New Mexico, $2n=48$, (9) Redondo, Jemez Mountains (RD, JM), N New Mexico, $2n=48$, (10) Las Conchas, Jemez Mountains (LC, JM),

N. New Mexico, $2n=48$, (11) Mount Taylor (MT), N. New Mexico, $2n=48$. Karyotypes 48 Wyoming (=48 W), 46 and 44 are represented each by one population only. Karyotypes $2n=40$ and $2n=60$ are represented by two isolated populations each, while $2n=48$ New Mexico (=48 NM), which differs in morphology from $2n=48$ W, is represented by four populations, CN, RD–LC (both in the Jemez Mountains, separated altitudinally) and MT. CN is isolated from (RD+LC) and they are both isolated from MT. Detailed accounts of all localities are given in ref. 5. Thaeler (ref. 6 and unpublished work) has shown in extensive karyotypic analysis of the *Thomomys talpoides* complex that where numerous differences in karyotype exist, either in number or morphology of chromosomes, the karyotypes coexist parapatrically with little or no interbreeding. From this he assumes, on distributional evidence, that the six karyotypes involved in this study represent at least five distinct species whose diploid numbers are $2n=48$ W, 44–46 (which may or may not be conspecific, no evidence is yet available), 40, 60 and 48 NM.

The distribution of commonest allele at twenty-four polymorphic loci in the eleven populations, together with their respective $\hat{F}_e$ values are given in Table 1. The loci in Table 1 are arranged in three groups[8]: Group I, glucose metabolizing enzymes, Group II, all other enzymes, and Group III, nonenzymatic proteins. Alleles are designated alphabetically in order of decreasing mobility of their alloenzymes. Of the thirty-one loci examined eight are monomorphic in all eleven populations for the same allele, seven are fixed for the same

Table 1 Frequency of Commonest Allele at Twenty-four Polymorphic Loci in Eleven *Thomomys talpoides* Populations Together with their $\hat{F}_e$ Values

Locus and allele*			SR	WC	DH	TF	KP	LS	ML	CN	JM† RD	JM† LC	MT	Effective inbreeding coefficient ($\hat{F}_e$)‡
		$2n=$	48	46	44	40	40	60	60	48	48	48	48	
		N =	(30)	(30)	(26)	(24)	(30)	(24)	(25)	(30)	(14)	(15)	(28)	
Group I: glucose metabolizing enzymes														
Mdh-1	a		1.0	1.0	1.0	0.98	1.0	0.94	1.0	1.0	1.0	1.0	1.0	0.059
aGpd	b		1.0	0.95	1.0	1.0	1.0	1.0	1.0	0.95	1.0	1.0	1.0	0.041
Ldh-1	b		1.0	0.90	1.0	1.0	1.0	1.0	0.98	0.00	0.00	0.00	0.00	0.957
Ldh-2	b		1.0	0.87	0.90	1.0	1.0	0.92	1.0	1.0	1.0	1.0	0.70	0.155
Idh-1	b		1.0	1.0	1.0	1.0	0.65	1.0	1.0	0.98	1.0	1.0	0.00	0.794
6Pgd	b		1.0	1.0	1.0	1.0	1.0	0.35	0.00	1.0	0.93	0.73	0.91	0.658
Got-1	c		1.0	1.0	1.0	1.0	0.90	1.0	1.0	0.98	1.0	1.0	1.0	0.077
Got-2	a		1.0	1.0	0.98	1.0	1.0	1.0	1.0	0.98	1.0	1.0	1.0	0.017
Pgm	c		0.88	0.92	1.0	1.0	0.00	1.0	1.0	1.0	0.89	0.89	1.0	0.696
Pgi	a		1.0	1.0	1.0	1.0	1.0	0.65	1.0	1.0	1.0	1.0	1.0	0.329
Tpi	b		1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.88	0.71	0.60	1.0	0.265
Group II: other enzymes														
Sdh	a		1.0	1.0	1.0	0.92	1.0	0.98	1.0	0.98	1.0	1.0	1.0	0.050
Pept	b		0.52	1.0	0.98	1.0	0.00	1.0	0.88	1.0	1.0	1.0	1.0	0.729
Acph	b		0.68	1.0	1.0	0.98	1.0	0.19	1.0	0.98	1.0	1.0	1.0	0.607
Es-2	b		1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.55	0.36	0.33	0.14	0.589
Es-3	b		1.0	0.85	0.73	0.63	0.22	0.58	0.98	0.98	0.61	0.50	0.68	0.249
Es-4	c		0.45	0.92	0.96	0.77	0.00	0.88	0.98	0.87	1.0	0.93	0.91	0.495
Ak-1	a		1.0	1.0	1.0	1.0	0.00	1.0	1.0	1.0	1.0	1.0	1.0	0.091
Ak-2	c		1.0	0.72	0.98	0.00	1.0	0.00	0.00	1.0	0.96	0.97	1.0	0.081
Group III: nonenzymatic proteins														
Hb	b		1.0	1.0	0.90	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.092
Preal-1	b		1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.65	0.93	1.0	0.55	0.326
Preal-2	a		1.0	0.98	0.92	1.0	1.0	0.83	1.0	1.0	0.96	1.0	1.0	0.094
Alb	a		0.00	0.62	0.73	1.0	1.0	1.0	1.0	0.00	0.00	0.00	0.52	0.750
Trf	b		1.0	1.0	0.98	1.0	1.0	0.94	1.0	0.98	1.0	0.96	1.0	0.361

Proteins are arranged in three groups: *group I*, glucose metabolizing enzymes, *group II*, other enzymes; *group III*, nonenzymatic proteins.

* Abbreviations: *Mdh-1* malate dehydrogenase 1, *aGpd* alpha glycerophosphate dehydrogenase, *Ldh-1*: Lactate dehydrogenase-1; *Ldh-2*: Lactate dehydrogenase-2, *Idh-1*: Isocitrate dehydrogenase-1; *6Pgd* 6 phosphogluconate dehydrogenase; *Got-1* and *2*: Glutamic-oxaloacetic transaminase 1 and 2; *Pgm*: Phosphoglucomutase, *Pgi*: Phosphoglucose isomerase; *Tpi* Triosophosphate isomerase; *Sdh*: Sorbitol dehydrogenase, *Pept*: Peptidase, *Acph*: Acid phosphatase, *Es-2*: Esterase-2, *Es-3* Esterase-3; *Es-4*. Esterase-4, *Ak-1*: Adenylate kinase-1, *Ak-2*: Adenylate kinase-2, *Hb*: Haemoglobin, *Preal-1*: Prealbumin-1; *Preal-2* Prealbumin-2; *Alb*: Albumin; *Trf*: Transferrin.

† JM involves two subpopulations.

‡ Corrected for sampling error by subtracting $1/n=0.04$ from the observed $\hat{F}_e$, mean $n=25$.

Table 2 Summary of Four Tests for the Heterogeneity of $\hat{F}_e$ by Comparison of Observed and Theoretical Variances for all Major Alleles and Three Groups of Proteins in *Thomomys talpoides*

Group	Alleles (N)	Effective inbreeding coefficient Observed* mean ($\bar{F}$)	Observed* variance (S^2_F)	Theoretical (σ^2)	S^2_F/σ^2	Critical F value with appropriate degrees of freedom	P
All major alleles	24	0.317	0.079	0.020	3.94	$F0.001(23,\infty)=2.13$	<0.001
Group I (Glucose metabolizing enzymes)	11	0.328	0.119	0.021	5.52	$F0.001(10,\infty)=2.84$	<0.001
Group II (Other enzymes)	8	0.321	0.066	0.021	3.19	$F0.001(7,\infty)=3.47$	<0.005
Group III (Nonenzymatic proteins)	5	0.285	0.072*	0.016	4.47	$F0.001(4,\infty)=4.62$	<0.005

* Corrected for sample size

allele (*Mdh-2, Idh-2, Adh, Ipo, Es-5, Prot-1* and *Hp* (these do not appear on Table 1), while Ak-1 is fixed for the same allele in nine populations but for an alternative one in the KP population (Table 1). Most loci tend to monomorphism in reproductively as well as geographically isolated populations. This results in relatively low heterozygosity ($\bar{H}$), 0.047 (range, 0.008–0.085), which is even lower if the highly polymorphic esterases (*Es-3* and *Es-4*) are excluded ($\bar{H}=0.037$, range, 0.005–0.067) A remarkable feature is the weak regional polymorphism in most populations Most loci, either monomorphic or weakly polymorphic have the same, either fixed or predominant allele Alternative fixation between or within karyotypes, is relatively uncommon Finally, high genic similarity characterizes karyotypes[5]

The $\hat{F}_e$ values are distinctly heterogeneous, running from very low to very high values. This apparent heterogeneity of $\hat{F}_e$ was tested by comparing the observed (corrected for sampling error) and theoretical variances first for all twenty-four alleles, then for each of the above mentioned protein groups separately, the results are summarized in Table 2 The test performed was the conservative one using $k=2.0$ for deriving the theoretical variance, which is appropriate for binomial gene distribution[3] The number of populations in the analysis is $n=11$, from this the theoretical variance, $\sigma^2=k\bar{F}/n\text{-}1$ was calculated by $\sigma^2=2.0\,\bar{F}^2/10$, where $\bar{F}$ or mean $\hat{F}_e$, is given for each group separately in Table 2 The ratios between the observed and theoretical variances of inbreeding coefficients is also given in Table 2 together with the critical values of the F distribution, which is distributed as x^2/d f [3]

The ratio of observed and theoretical variance (Table 2) indicates excess heterogeneity of $\hat{F}_e$ values for all alleles tested as well as for each of the three protein groups The ratio decreases from group I to III and then group II, being 5.52, 4.47 and 3.19, respectively This heterogeneity can be taken as evidence for selection Furthermore, the differences in the values of $\hat{F}_e$ may suggest the type of selection operating[3]. Uniform selection across the range will result in a low variance and so in low $\hat{F}_e$ values This is certainly true for alleles which are either prevalent or close to fixation across populations (*Mdh-1, aGpd, Got-1, Got-2, Sdh, Ak-1* and the monomorphic loci which are not analysed here as they do not vary across the range) On the other hand, diversifying selection will result in high variance among populations, suggesting differential selection in different environments This seems to be the case in the strongly polymorphic loci (esterases) a fact which is displayed by the geographical, clinal variation of *Es-2* and *Es-3* High $\hat{F}_e$ values also occur when alternative fixation of alleles takes place either among karyotypes (*Ldh-1, Alb*) or among populations within a karyotype (*Idh-1, 6Pgd, Pgm, Pept*)

The ranking of heterogeneities of $\hat{F}_e$ is group I > group III > group II. This finding is inversely correlated with mean heterozygosity per individual ($\bar{H}$) which is 0.037, 0.042 and 0.061 respectively[5] The differential $\bar{H}$ found among the three groups, particularly between groups I and II, is consistent with similar findings in *Drosophila*[7–9], though apparently inconsistent with data for vertebrates[10] Gillespie and Kojima[7] predicted that glucose metabolizing enzymes would be less variable than peripheral enzymes because their physiological function is more specific than that of group II enzymes Further support for the hypothesis that the three protein groups may partly be under differential selective pressures is suggested by a multiple regression analysis of the variance in their $\bar{H}$ (ref 5).

The six karyotypes studied are distinctly similar genetically, $I^{11}=0.925$ (range, 0.859–0.996) (ref 5), yet migration can be completely ruled out to explain similarities First, field evidence suggests complete reproductive isolation between karyotypes such as $2n=60$ and $2n=48$ NM (populations ML and CN), or between $2n=60$ and $2n=48$ NM (populations ML and CN), or between $2n=44$ and $2n=40$ (DH and TF), and nearly so between $2n=46$ and $2n=48$ W (ref. 6 and C S Thaeler, unpublished) Second, the isolated populations at the southernmost fragmented portion of the *T talpoides* range (KP, LS, JM, MT) are completely isolated geographically on mountain tops, with vast intervening lowlands occupied by *Thomomys bottae* which competitively excludes, and is reproductively isolated from *T talpoides*[12]. The genic similarity among the six karyotypes, despite their reproductive and/or geographical isolation strongly supports selection as an important cause of genetic differentiation in *Thomomys talpoides* populations

The general pattern of low heterozygosity that characterizes pocket gophers as well as other fossorial rodents[13] is best explained as an adaptive strategy for homozygosity in the relatively uniform, but narrow-niche underground environment Strong selection for homozygosity may particularly be operating on alleles which did not diverge across the range in spite of reproductive and ecogeographical isolations in the late and post-Pleistocene period.

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Number of Gene Loci required for Accurate Estimation of Ancestral Population Proportions in Individual Human Hybrids

GENETIC studies giving estimates of the Caucasian genetic contribution to American blacks have recently been reviewed and extended[1] These group admixture estimates are mean population values, but estimates of admixture proportions for individuals of hybrid origin, using genetic markers, have not been published Recent interest in this possibility, however, has led to an explicit proposal for making such individual estimates[2,3] This communication is not concerned with the reasons for making such estimates nor with the uses to which they may be put Its purpose is to demonstrate, by a simple argument, that the number of genetic marker loci required for reasonably accurate individual admixture estimates seems to be so large that such estimates cannot be made now or in the near future

To make the argument as simple as possible and avoid intractable complexities (which we discuss later), I postulate an ideal estimation situation Because real estimation will not be as favourable, the estimate from the ideal model of the number of loci will necessarily represent the minimum. We make the following five assumptions. (i) The hybrid population H is derived from two genetically different ancestral populations, P_1 and P_2. (ii) There is negligible selection, mutation, and genetic drift at the marker loci used in estimating μ_i (the true proportion of genes in the *i*th individual in *H* which derive from P_1, m_i is an estimate of μ_i). (iii) The marker loci used for estimating μ_i are representative of all loci in indicating population origin. (iv) Each allele at each marker locus in a person in *H* is individually classifiable, without error, as coming from either P_1 or P_2 (that is, there is no dominance, epistasis, or misclassification and P_1 and P_2 are homozygous, for different alleles, at each marker locus). (v) The marker loci used assort independently at meiosis (there is no close, moderate, or loose linkage between any pair of these loci so that each locus gives an equal, independent, and maximal amount of information about ancestral population origin). Because we are not concerned here with the processes which have produced a given μ_i, we need say nothing about the mating patterns in *H*.

Given that these five assumptions hold, a person with *n* ideal marker loci has 2*n* ideal genes, each classifiable as coming from P_1 or P_2. m_i, estimating μ_i, is therefore the proportion of these 2*n* genes coming from P_1. The variance of m_i, s_i^2, is $u_i(1-\mu_i)/2n$. We can specify the accuracy of m_i by its standard error, s_i. Therefore,

$$n=\mu_i(1-\mu_i)/2s_i^2 \tag{1}$$

For a specified s_i, which we may call *s*, *n* varies with $\mu_i(1-\mu_i)$. μ_i, in persons in *H*, can vary between 0 and 1 and $\mu_i(1-\mu_i)$ has its maximum when $\mu_i=0.5$. The expected value of μ_i is about 0.22 for non-Southern American blacks and about 0.1, or slightly more, for most Southern American blacks[1]. To ensure that the estimate of *n* for a majority of American blacks is usually a minimum estimate, *n* is estimated with $\mu_i=0.1$. For such a minimum estimate, n_{min} therefore

$$n_{min}=0.045/s^2 \tag{2}$$

The value of *s* for "accurate" estimation depends on the definition of "accurate" and is necessarily arbitrary. In my opinion *s* should not exceed 0.05, corresponding to a 95% confidence interval of about 0.20.

Using $s=0.05$, equation 2 estimates n_{min} to be eighteen ideal loci (thirty-six ideal genes). For this number, a m_i of 0.10 has a 95% confidence interval of about 0.025–0.25 (ref. 4). This minimum estimate gives only minimal accuracy. If we wish to reduce the 95% confidence interval to a width of about 0.10, corresponding to $s=0.025$, we would require (for $\mu_i=0.1$) seventy-two ideal loci as a minimum. To interpret these estimates we note that only one or two known marker loci of man approach the ideal in population discrimination. Even the best population marker, the *Gm* locus, falls short of having high frequency, distinctive alleles in each major racial group[5]. When comparison is only between African populations ancestral to American blacks (West Africa and the western coast, south to Southwest Africa[1]), and Caucasians, and detailed testing is done, *Gm* is almost ideal because neither population shares common alleles[5]. The Duffy locus is almost as good for this comparison when both anti-Fy^a and anti-Fy^b are used[1]. Most of the approximately fifty marker (polymorphic) loci known in man make much less sharp distinctions for this comparison or for other racial comparisons.

The relative usefulness of a particular gene *g*, present in a dihybrid individual *I*, for providing information on the ancestral population origins of that gene is a simple function of the frequencies of *g* in the two ancestral populations. The following illustration shows how greatly two genes, each seemingly discriminative, may differ from each other in their usefulness for discriminating between such ancestral populations. The frequencies of the Fy^a gene of the Duffy blood group system in Caucasians and Africans (of the former slaving areas) are about 0.43 and about 0.01, respectively, while the corresponding frequencies of the *A* gene of the ABO blood group system are about 0.40 and 0.15[1,6]. The population difference for Fy^a is less than twice that of *A* but, for the simplest case of $\mu_i=0.5$, Fy^a is about sixteen times more informative (comparing likelihood ratios) than *A* with regard to population origin. The Fy^a gene is, in fact, probably the best single gene discriminator now available for these two populations[1]. This great superiority of Fy^a over *A* for individual admixture estimates in American blacks parallels a similar finding (Fy^a gives twenty-two times more information than *A*) for group admixture estimates[1].

These calculations emphasize how far short of ideal most genetic markers are for making racial distinctions. The minimum requirement of eighteen ideal loci for the majority of American blacks (those with μ_i greater than 0.1) means that, contrary to the suggestions of some authors[2,3], accurate individual estimates of admixture, using genetic markers, are not now possible for this or any other human hybrid population, although for some purposes, such as study of hypertension in a hybrid population where ancestry may be important[2], estimates of individual admixture may be useful for reducing unexplained variation, even though they are not individually accurate.

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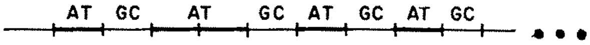
Model for Evolutionary Origin of Chromosome Bands

MANY eukaryotic chromosomes stained with quinacrine or by one of the Giemsa banding techniques show numerous bands in the chromosome arms. These have been termed Q or G-bands[1]. Autoradiographic studies show they correlate well with late replicating heterochromatin[2] and a number of biochemical and immunological procedures indicate the DNA in these regions is relatively AT-rich[5-7]. This raises the following enigma: as each banded region has enough DNA to hold several thousand genes[5] how is it possible for a given region of the chromosome to accumulate enough AT-rich genes to lead to a discernible band?[7] In view of the rather gross folding pattern of chromatin in mitotic chromosomes[8] only a markedly non-random distribution of AT-rich regions could produce banding.

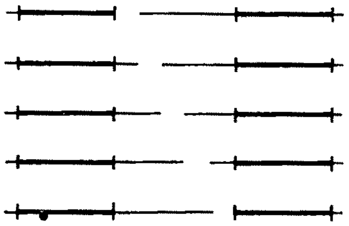
Some people have suggested the answer to be that the AT-rich banded regions are composed of repetitious sequences[5,9]. While it is true that the C-band regions[1,10] are usually enriched in repetitious satellite DNA, several observations suggest that this is not true for the intercalary heterochromatin in the Q and G-bands.

First, the Chinese hamster possesses many C and G-bands but very little satellite DNA[11], its early replicating DNA is no more repetitious than its late replicating DNA[12], and its isolated heterochromatic DNA is no more repetitious than its isolated euchromatic DNA[11] Second, the moderately repetitious sequences seem to be distributed throughout the nonrepetitious sequences[13] Further evidence for this comes from electron microscopy of moderately repetitious DNA reannealed to non-repetitious DNA which shows no evidence for clustering of the moderately repetitious sequences in *Drosophila*[14] or rats (personal communication from D Holmes and M Wilkes) Third, *in situ* hybridization has not yet provided any evidence for the clustering of repetitious sequences in the Q or G-band regions

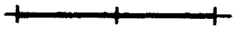
If the non-random distribution of AT-rich DNA is not due to repetitious sequences, how can it be explained? The answer may lie in the recent observation by Seabright[15] that X-ray-induced breaks tend to occur predominantly in interband regions This suggests that there is some characteristic of the AT-rich intercalary heterochromatin[7,8,16] which protects it from radiation-induced (and probably sporadic) breakage If confirmed, this single characteristic would be sufficient to account for the non-random accumulation of intercalary heterochromatin Thus, a primitive organism may start with a stretch of DNA in which AT-rich inactive heterochromatic regions and relatively GC-rich active genes are evenly dispersed



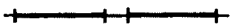
If breakage occurs in the GC-rich regions the following types of breaks will occur



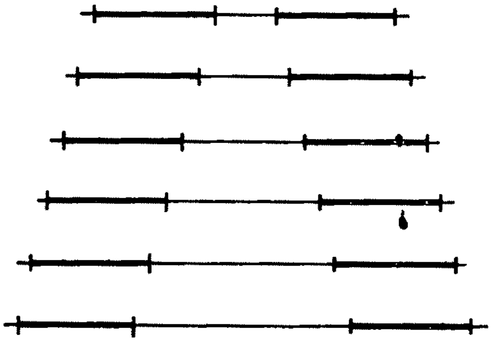
Subsequently, the following types of reunions will occur (*a*) those with fusion of heterochromatic regions,



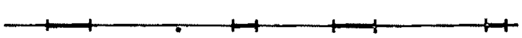
(*b*) those with almost fused heterochromatin,



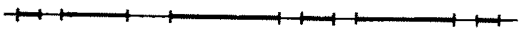
and (*c*) those with fused euchromatin



Because of the decreased breakability in heterochromatin, types *a* and *b* would tend to persist, while type *c* would continue to undergo further breaks This would eventually lead to the non-random accumulation of AT-rich heterochromatin and relatively GC-rich euchromatin sufficient to result in detectable banded regions Presumably the separation would be far from perfect and the euchromatin would contain numerous small segments of AT-rich heterochromatin,



and the heterochromatin would contain numerous regions of relatively GC-rich euchromatin



This would be consistent with the stability of the banded regions[17,18] and the observation that many more bands are present in chromosomes that are extensively despiralized[19]

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Nitrogen Fixation in Termites

SOME termites can live on a diet of cellulose filter paper[1] This characteristic prompted Hungate[2] to question the possibility of N_2 fixation in termites by estimating the N balance of growing termite colonies, but he found no net increase in total colony N Tóth[3], on the other hand, incubated macerated termites in an N-free organic medium and observed an increase in fixed N in the solution He used long incubation times, however, and possibly selected for N_2-fixing organisms in the medium We decided to reinvestigate the question of N_2 fixation in termites by exploiting the sensitivity of the acetylene reduction assay, a reliable indicator of N_2 fixation[4,5] Preliminary reports of these results have already been published[6,7]

Fifty workers of the subterranean termite, *Coptotermes formosanus* Shiraki, assayed immediately on removal from a nest of wood, were placed in a 10-ml vial containing 12 µmol C_2H_2 Ethylene, as measured by gas chromatography[5], was produced at a rate of 0 122 nmol h^{-1} C_2H_4 formation was dependent on the presence of C_2H_2, and was proportional to the number of termites used All termites remained alive during the experiment, but the rate of C_2H_4 formation decreased with time, perhaps owing to some toxicity of C_2H_2 for the termites Consequently, we routinely used a standard incubation of 1 h at 30° C to obtain initial reaction rates

The hindgut of many termites is packed with cellulose-digesting protozoa, and bacteria such as spirochaetes, and is the site of considerable microbial activity[8] It thus seemed likely that it was also the site of N_2 fixation When the guts of intact termites were removed[9] and assayed, C_2H_2-reducing activity was associated with the guts No activity was asso-

Table 1 Effect of Diet on C_2H_2-reducing Activity of *C formosanus*

Diet	Specific activity*	No of bacteria per gut
Wood (colony)	0 122±0 048	2.6×10^6
Additions to Whatman No 2 filter paper†		
No additions	1 310	$3\ 4\times10^6$
$(NH_4)_2SO_4$		
0 8 mg	0 810	Not determined
8 0 mg	0 007	Not determined
KNO_3		
1 2 mg	0 197	Not determined
12 0 mg	0 007	Not determined
Antibiotics‡	0 000	$0\ 0\times10^6$

* C_2H_4 (nmol) formed from C_2H_2 per 50 termites per h, determined after 10 d feeding

† All filter disks were impregnated with 0 6 ml of a basal salts mixture containing (mg per 100 ml distilled water) KH_2PO_4, 30, $MgSO_4\ 7H_2O$, 20, $MnSO_4\ H_2O$, 2, $CaCl_2\ 2H_2O$, 5, $Na_2MoO_4\ 2H_2O$, 1×10^{-2}, $FeCl_3$, 0 2, $ZnSO_4\ 7H_2O$, 1×10^{-2}, $MnCl_2\ 4H_2O$, 3×10^{-3}, H_3BO_3, 3×10^{-2}, $CoCl_2\ 6H_2O$, 2×10^{-2}, $CuCl_2\ 2H_2O$, 1×10^{-3}, and $NiCl_2\ 6H_2O$, 2×10^{-3} The *p*H of the solution was adjusted to 7 0 with NaOH Termites were transferred to fresh filter disks after 7 d

‡ Tetracycline, 480 µg, penicillin, 540 µg, chloramphenicol, 600 µg, and streptomycin sulphate, 600 µg

ciated with de-gutted termite bodies The C_2H_2-reducing activity of guts was only about 16% that of the intact termites, and undoubtedly reflected less-than-optimal assay conditions in the vial These data suggested that microbes present in the alimentary tract were responsible for C_2H_2 reduction in termites

The C_2H_2 reduction assay for N_2 fixation is based on the behaviour of C_2H_2 as an analogue of N_2, and its reduction to C_2H_4 by nitrogenase[4] Significant catalysis of C_2H_2 to C_2H_4 is known only in those biological systems capable of fixing atmospheric N_2 Nevertheless, we sought further to establish that C_2H_4 formation from C_2H_2 by termites actually represented N_2 fixation Direct demonstration of an enrichment of combined ^{15}N from an atmosphere enriched with $^{15}N_2$ (ref 10) was not possible because of the relatively low C_2H_2-reducing activity of termites Nitrogenase synthesis (and from this C_2H_2-reducing activity) by all N_2-fixing systems studied, however, is known to be repressed when NH_4^+ is included in the growth medium[11], and this therefore affords an alternative test We attempted to determine if the C_2H_2-reducing activity of termites would be decreased by feeding them a diet supplemented with NH_4^+ or other N-containing compounds Groups of 50 *C formosanus* workers were placed in glass Petri plates each containing a 7-cm circle of Whatman No 2 cellulose filter paper Filters were impregnated with an aqueous trace salts solution with or without the inclusion of a N-source and the termites were incubated with the moist filters at 25° C for 10 d Termites readily ate the filters, and similar amounts of paper were consumed by each group The termites were then assayed for C_2H_2-reducing activity (Table 1) Termites fed filter paper containing no added N-source had more than ten times greater C_2H_2-reducing activity than termites fed wood Presumably the filter disks contained less combined N than wood from the termite nest Addition of NH_4^+ or NO_3^- to filters diminished C_2H_2-reducing activity to an extent

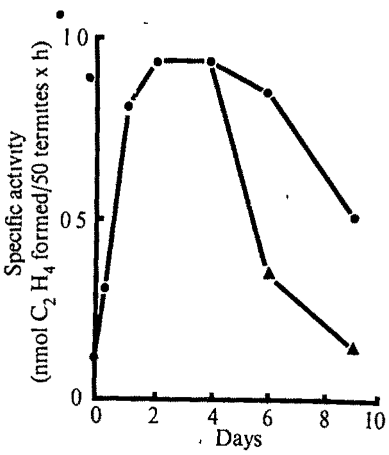

Fig. 1 Modulation of C_2H_2-reducing activity of *C formosanus* by dietary NH_4^+ Two groups of fifty workers each were fed Whatman No 2 filter paper moistened with a basal salts mixture (see Table 1) On day 4 one group was transferred to fresh filter paper impregnated with basal salts plus 8 0 mg $(NH_4)_2SO_4$, (▲), the other group was transferred to fresh filter paper containing basal salts with no added $(NH_4)_2SO_4$ (●) Specific activities up to 4 d were averages of the two groups

Table 2 N_2 (C_2H_2) Fixation in Termites and Other Insects

Termite	Caste	Diet	C_2H_4 nmol formed per h Per 50 termites	C_2H_4 nmol formed per h Per g termites
Coptotermes formosanus	Worker	Wood (colony)	0 122	0 695
	Soldier	Wood (colony)	0 027	0 139
Reticulitermes flavipes	Worker	Wood (colony)	0 043	0 204
	Soldier	Wood (colony)	0 014	0 073
Zootermopsis sp	Reproductive nymphs and workers	Wood (colony)	0 517	0 272
Cryptotermes brevis	Reproductive nymphs	Moist filter paper (12 h)	0 622	1 705

The following insects formed no detectable C_2H_4 from C_2H_2

Insect*	Common name	Sex†	No of insects per assay
Acyrthosiphon pisum	Pea aphid	ND	50
Attagenus megatoma	Black carpet beetle	M, F	50
Blattella germanica	German cockroach	ND	10
Camponotus sp	Carpenter ant	Mixed	16
Dermestes maculatus	Hide beetle	Mixed	10
Drosophila melanogaster	Fruit fly	Mixed	50
Lasioderma serricorne	Cigarette beetle	Mixed	48
Mezium americanum (adults and larvae)	Spider beetle	ND	50
Musca domestica	House fly	Mixed	15
Oncopeltus fasciatus	Milkweed bug	ND	30
Periplaneta americana	American cockroach	ND	1
Rhyzopertha dominica	Lesser grain borer	ND	50
Stegobium paniceum	Drugstore beetle	ND	50
Supella supellectilium	Brown-banded cockroach	ND	10
Tenebrio molitor (larvae)	Yellow mealworm	ND	2
Tribolium confusum	Confused flour beetle	Mixed	50
Trogoderma inclusum	Large cabinet beetle	M, F	50

* Adult insects were assayed unless indicated otherwise

† M=male, F=female, mixed=males and females together, ND=not determined

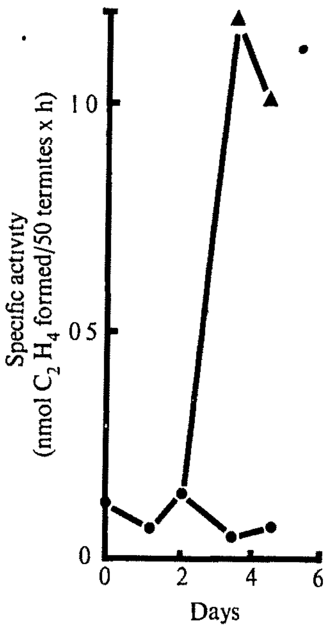

Fig. 2 Modulation of C_2H_2-reducing activity of *C formosanus* by dietary NH_4^+ Experiment performed in a manner similar to that of Fig 1 except termites were begun on a diet of filter paper impregnated with basal salts plus 8 0 mg $(NH_4)_2SO_4$ (●) Termites were transferred to fresh paper without added $(NH_4)_2SO_4$ on day 2 (▲)

which varied with the amount of N-compound impregnated on the filter Addition of high concentration of N-compound to filters diminished C_2H_2-reducing activity below that of termites fed wood Similar depression of C_2H_2-reducing activity was affected by impregnating autoclaved *Escherichia coli* (10^9 cells) or aspartic acid (120 mg) on filters used for feeding These data indicate that the C_2H_2-reducing activity of termites is modulated by the amount of N contained in the diet, and offer strong evidence that C_2H_2 reduction in termites is mediated by nitrogenase

When termites were fed filter disks containing antibacterial antibiotics, all detectable C_2H_2-reducing activity was abolished This was parallelled by a loss of detectable bacteria (but not protozoa) from the hindgut (Table 1) Protozoa eventually disappeared after 20 d or longer These data are consistent with the idea that prokaryotes in the termite gut are responsible for N_2 fixation, and suggest that intestinal bacteria also influence the vitality of the protozoa

The increase in C_2H_2-reducing activity of termites fed filter paper probably represents derepression of nitrogenase synthesis by gut bacteria rather than marked proliferation of N-fixing organisms possessing constant levels of enzyme The relatively small increase in the total number of gut bacteria (31%) compared with the dramatic increase in nitrogenase activity (974%) (Table 1) is consistent with this interpretation Whether the marked diminution of C_2H_2-reducing activity by NH_4^+ represents elimination of N_2-fixing bacteria from the gut, or degradation of pre-existing nitrogenase, cannot be concluded at present Microscopic examinations, however, revealed an abundance of bacteria and protozoa in guts of termites fed NH_4^+-impregnated paper for 10 d, suggesting that if N_2-fixers are eliminated, other bacteria proliferate

We evaluated the efficiency of the N_2-fixing system in *C formosanus* by periodically measuring their C_2H_2-reducing activity after changing their dietary N content (Fig 1) The N_2-fixing activity in *C formosanus* increases rapidly when the termites are fed filter paper, a diet presumably low in combined N A significant increase in C_2H_2-reducing activity was observed after 5 h of feeding maximum activity was attained after 2–4 d When filter paper-fed termites were transferred to fresh filter disks containing NH_4^+, C_2H_2-reducing activity diminished sharply compared with a control group of termites transferred to fresh disks with no added NH_4^+ C_2H_2-reducing activity of filter paper-fed termites also decreased, although more slowly The 9-d specific activity of the filter paper-fed termites was lower than that generally observed (see Table 1) The specific activity of C_2H_2-reduction in termites fed filter paper for 25 d decreased to 0 216 This was paralleled by an observable decrease in the termites' feeding rate, and undoubtedly reflected a response to the rather unnatural environmental conditions imposed on these subterranean termites

In a reciprocal experiment, termites were fed a diet of filter paper+NH_4^+ and then transferred to disks containing no added NH_4^+ (Fig 2) This resulted in a rapid increase in C_2H_2-reducing activity, whereas the NH_4^+ control group maintained low levels of nitrogenase activity These data indicate that nitrogenase activity in *C formosanus* responds rapidly to changes in dietary N content The rapidity of the response is probably limited primarily by the time required to significantly change the concentration of ingested N in the gut In termites studied, food passage through the gut takes about a day[8] On the basis of our studies of the time course modulation of C_2H_2-reducing activity therefore we consider the N_2-fixing system of *C formosanus* to be efficient, and potentially able to supply the termite quickly with combined N should the dietary level suddenly drop

To determine the distribution of $N_2(C_2H_2)$ fixation in insects, we assayed different termites, as well as representatives of seventeen genera of insects available from laboratory cultures, for their C_2H_2-reducing ability Of all insects tested, only termites reduced C_2H_2 to C_2H_4 (Table 2) All castes of termites tested reduced C_2H_2 to C_2H_4, but soldiers possessed the lowest activity This was not unexpected because soldiers do not feed on wood as do workers instead, they periodically obtain stomodaeal and proctodaeal nutrients from colony mates[12] The relatively high C_2H_2-reducing activity of *Cryptotermes brevis* Walker was probably due to their feeding on paper for 12 h before assay

N_2-fixing bacteria, or their metabolic products, may serve directly as a N-source for the termites It is also possible, however, that the termites obtain all their N from ingested wood, and merely obtain growth factors from the N_2-fixing bacteria, or from protozoa which might require N_2-fixing bacteria

Termites are of obvious economic concern Worldwide termite damage and control costs are estimated at 1 2 billion dollars annually[13] On the other hand, termites are important ecologically In natural environments, they play a role in the turnover of complex carbohydrates by degrading dead trees and other cellulose-containing materials to more simple carbon compounds They also increase soil aeration and drainage In view of the ability of their microbial symbionts to fix atmospheric N_2, termites may also play a hitherto unrecognized role in soil fertility by replenishing combined N compounds in the soil This may be particularly significant in tropical regions where termites abound

We are now attempting to isolate the bacteria responsible for N_2 fixation in termites, and to evaluate the relevance of symbiotic N_2 fixation to the vitality of the insect The latter may have significant economic implications If, for example, N_2 fixation is indispensible for termite vitality, suppressive measures may be directed toward destroying the integrity of the N_2 fixation system in these insects

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Erratum

IN the article "Significance of Lead Isotope Composition in the Blood" by W I Manton (*Nature*, **244**, 165, 1973) the axes of the figures were wrongly labelled during preparation for the printers The corrected figures are reprinted below

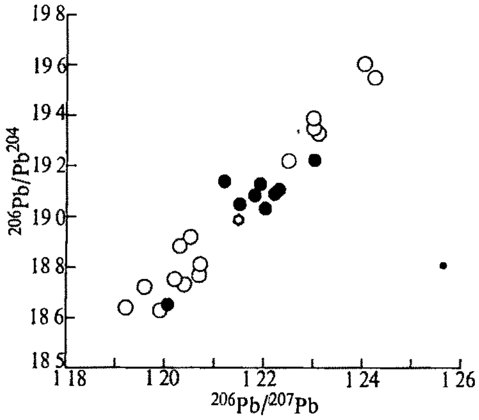

Fig. 1 Isotope ratios of lead in petrol collected in Dallas on July 14, 1972 (○), and of airborne particulate lead collected at various stations on July 18, 1972 (●) o, Mean of the gasoline

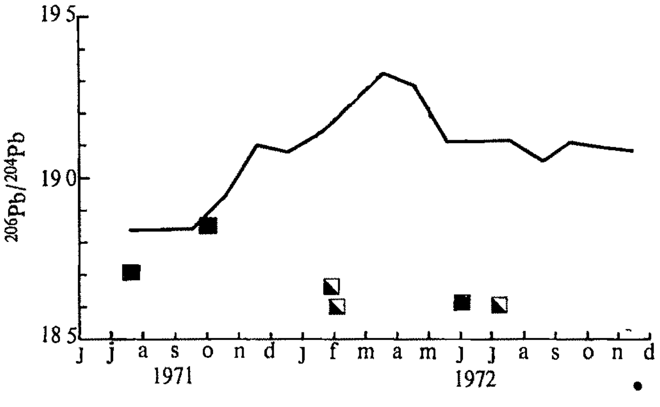

Fig. 2 ^{206}Pb/^{204}Pb ratio of airborne particulate lead over Dallas as measured from one station at monthly intervals (—) Also shown are ^{206}Pb/^{204}Pb ratios from two smelters in the area (◩, ■)

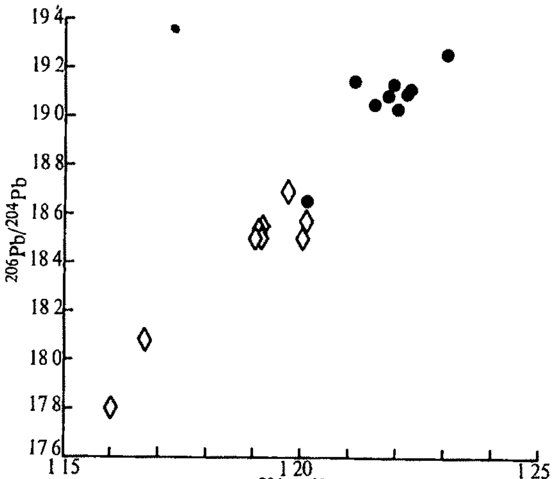

Fig 3 Isotope ratios of airborne particulate lead over Dallas on July 18, 1972 (●), and blood of Dallas residents (◇) drawn in August 1972

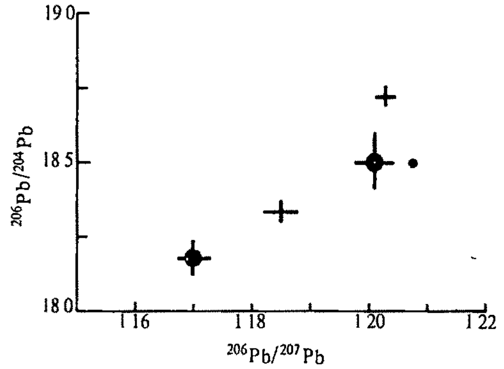

Fig. 4 Isotope ratios of blood of spouses W M and J M (+) and B C and T C (●) Bars represent 95% confidence limits

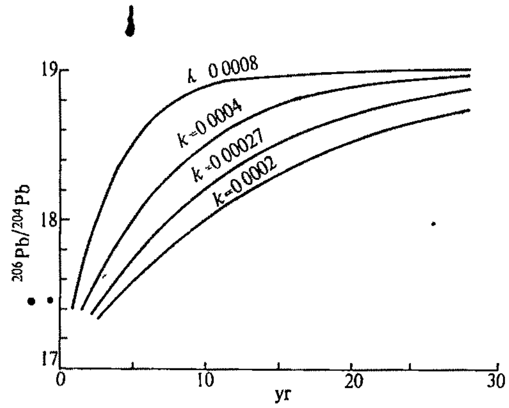

Fig 5 Change in the ^{206}Pb/^{204}Pb ratio of lead in blood from an initial value of 17 because of the absorption of lead with a ^{206}Pb/^{204}Pb ratio of 19 Curves are shown for various values of *k*

BOOK REVIEWS

Newtonian Algebra

The Mathematical Papers of Isaac Newton Edited by D T Whiteside Volume 5 1683–1685 With the assistance of H A Hoskin and A Prag Pp xxii+627+4 plates. (Cambridge University London, July 1972) £20, $65

THE present volume of Dr Whiteside's magnificent edition of Newton's mathematical papers is concerned with the history of the work that was later to be published as the *Arithmetica universalis* In probably the first half of 1684 Newton, to comply with the statutes, deposited in the archives of Cambridge University a volume that purported to contain lectures on algebra delivered by him between 1673 and 1683 As Whiteside convincingly shows, the document can in no way represent a transcript of the lectures that Newton actually gave, and for at least one "lecture" Newton was not even in Cambridge at the stated time The document in fact had been heavily rewritten and divided somewhat arbitrarily into separate lectures, Newton's intent is clearly shown where at one point he inadvertently addresses himself to the "reader" But it seems that the work actually had few readers before it was published in 1707 by William Whiston, Newton's successor in the Lucasian Chair In 1722 a new edition was brought out which incorporated some revisions by Newton In neither of these editions did Newton's name appear on the title page, although the authorship would have been obvious The first edition was very favourably reviewed by Leibniz, but Whiteside finds that the work seems to have been little used until after Newton's death in 1727 It then had a certain vogue with further editions appearing, but was fairly soon to be superseded by other textbooks

The main bulk of this volume comprises an edition and translation of the deposited "lectures", but Whiteside also includes various preliminary drafts and intended revisions As with the previous volumes this one is greatly enriched by copious annotations, which give us the benefit of Whiteside's vast knowledge of seventeenth-century mathematical works, and he shows clearly how Newton incorporated various parts of his earlier work in this treatise—for example, notes that he had written for inclusion in the intended publication of Nicholas Mercator's Latin translation of a Dutch algebraic work by Gerard Kinckhuysen (The translation and Newton's notes were published in Whiteside's volume 2) My only regret is that the exigencies of producing the volume could not have allowed a rather easier system of cross-referencing In particular it is not always clear where information about changes made by Whiston for the 1707 edition or by Newton for the 1722 one will be found Thus the reader who notices an apparent lack of correspondence between some of the problems in this edition and those in the 1722 edition may well miss the fact that this is discussed on page 184 note 216

The treatise moves from elementary arithmetical operations to the algebraic treatment of quite complex problems But from the beginning Newton treats operations on numbers in close conjunction with those on "species" or letters denoting unknown or indeterminately treated quantities A central concern is the reduction of various problems to equations, which Newton explicitly regards as involving a translation from ordinary language to "algebraic language" Numerous problems are worked through as examples, and Newton pays particular attention to the use of algebra in the solution of geometrical problems. Considerable space is naturally also given to techniques for solving equations, and Newton enunciates various rules for identifying characteristics of roots of equations and the limits between which they will fall The last section of the work as it stands (Newton did not regard it as complete) treats of finding first approximations for numerical solutions of equations by mechanical geometrical constructions Here he reveals some doubts about the desirability of completely algebraicizing geometry, and maintains that "it is not the equation but the description that produces a geometrical curve" (page 424)

The nature of the material means that this volume brings to light less that is dramatically new about Newton than some of its companions. The meticulous scholarship that Whiteside has brought to it, however, helps to prepare for a fuller appreciation of Newton's algebraic work and reveals much concerning seventeenth-century approaches to this subject A G MOLLAND

Weisskopf on Physics

Physics in the Twentieth Century: Selected Essays By Victor F Weisskopf Pp xv+368 (MIT Cambridge, Massachusetts, and London, 1972) $7 95

IT was a good idea to collect in book form the most characteristic of Weisskopf's essays on topical problems of physics and the social issues that its unprecedented expansion has raised a source of renewed delight to his friends and pupils who already know its contents, this book provides to all enquiring minds and especially to the younger generation an introduction into the fundamental aspects of modern physics combining to a rare degree mastery of the subject with lucid simplicity of exposition Indeed, the refined quality of these essays and the charm of their style would have deserved a less shabby production The volume, introduced by a foreword (written by H Bethe with warm feeling and deep understanding) and a delightful autobiography, is divided into four parts, respectively dealing with the basic conceptual framework of quantum theory, the main problems of the constitution of atomic nuclei and of the still more "elementary" constituents of matter, more special issues connected with the same topics, and finally some philosophical and social questions On the latter the author discourses with his usual common sense, straightforwardness and generosity, but perhaps less pointedly than he used to do in our Copenhagen conversations with Placzek in the thirties Although it is going too far to describe Weisskopf (as Bethe does) as "an American with European background", it is undeniable that the American environment has left its mark on his European outlook There is one essay I sorely miss in this book it is the one Weisskopf has never written about the epistemological breakthrough brought about by quantum theory—a theme he is so well armed to treat with persuasive brilliance Confronted with the débâcle of epistemological thinking in the country of William James, why did he choose to shun the clamours of the Boeotians? L ROSENFELD

Nonscience

Cults of Unreason By Christopher Evans Pp 264 (George G Harrap London, July 1973) £3 net

THERE can be few who read this book who have not at one time or another had at least a mild brush with one of the cults or organizations whose history Dr Evans tells, scientology, flying saucers, blackboxery (particularly of the De La Warr variety) and eastern mysticism from Gurdjieff to Hare Krishna Dr Evans's thesis is straightforward and fairly familiar, the rationality of science has diminished the credibility of traditional western religions, yet men in an age of uncertainty need some sort of a creed. The need is filled by a variety of new cults, many of which have attempted to come to terms with science by incorporating real, or more often spoof, scientific elements into their *Weltanschauung* Having advanced the thesis, Dr Evans proceeds to illustrate it extensively from the history of scientology and its strange creator, L Ron Hubbard, from the Dianetics of the 1950s to today's incorporated "church of scientology" He then deals more briefly with some of the other fringe cults, hopefully fitting them into the same thesis.

For the sceptic the book is fun to read, Chris Evans has worked hard to assemble a set of cheerfully anecdotal histories, which succeed in putting down in turn each of these more barmy manifestations of religion as the opium of the people with a healthy dose of Anglo-Saxon empiricism and a wicked eye for revealing detail Believers, on the other hand, are scarcely likely to be convinced, if only because the author plays throughout the slightly unsatisfactory role of argumentation by story-telling Clear analysis of just what the scientologists and the flying saucer fans believe and why is sometimes sacrificed for the throw-away punch line Dr Evans could reasonably reply that he was not writing a "teach yourself scientology" or another addition to the burgeoning literature of Ufology, but the blurb promises us more not "a scientist's extended sneer at the intellectually inadequate (but) the bases of the truce between what we know and what we don't know"

This is where I think Chris Evans has chickened out, for he has not done this We never learn where he himself stands (except as an amused observer on the sidelines, watching the fans greet L. Ron as he arrives at Heathrow, or the shaven heads of the Hare Krishnas dancing down Oxford Street)

Clearly he does not "believe in" saucers, or Thetans, or the power of Yoga But what, if anything, does he believe in—other than the validity of the scientific method? Without this perspective, as a scientific enquiry the book is like Archimedes without his fulcrum As a sociological/philosophical enquiry, too, it lacks depth Is it enough to assert man's need for some type of belief system without exploring more fully who needs what and why? Who becomes a scientologist? Is it true that there is a class difference between the Hare Krishnas (working class) and the Black Boxers and Gurdjieffians (upper middle)? It is a pity that the author *does not* address himself a little to these questions, even at the speculative level.

There is one area of conspicuous omission, the most substantive "cult of unreason" today must surely be the conscious rejection of science, especially by the young, in search of an alternative mode of being à la Rozsak, a rejection of science undoubtedly occasioned by the very real oppressive role that it has come to play in the western world No hint of this critique of science comes through Dr Evans's account, and in that sense it is curiously out of touch with a large element of his theme. Nonetheless, the book is both brave—for the wrath of the cultists when aroused is notorious, and their arm often disturbingly long—and fun, an entertaining history of some of the minor twentieth century lunacies *Nature* readers should take it on holiday with them

STEVEN ROSE

Japonaiserie

Proteins Structure and Function. Edited by M Funatsu, K Hiromi, K Imahori, T Murachi and K Narita Volume 1 Pp x+381 £10 Volume 2 Pp x+270 £7 50 (Kodansha Tokyo, Halsted New York and London, April 1973)

ONE has become accustomed to publishers' *pots pourris* that contain collections of apparently unrelated items, linked only by the blurb writer's skill What unites the articles in *Proteins, Structure and Function*—and this must be accounted an ingenious gimmick—is that all the authors are Japanese The editors in their preface justify their selection by the suggestion that much of the Japanese work in protein chemistry is buried in domestic journals, sometimes in Japanese, and is therefore lost to colleagues working in the same field in the West They have therefore encouraged their authors to give personal rather than archival views of their subject, so as to reflect the interest and style of their own laboratories, and consequently a rather large proportion of the references throughout are to papers by themselves and other Japanese authors If this occasions a certain imbalance of treatment, it also makes for very readable accounts which specialists will for the most part welcome The choice of subjects is necessarily arbitrary, for not all aspects of protein chemistry are represented in Japan Volume 1 contains articles on enzymes of known sequence, trypsin, lysozyme, phage lysozymes and T_1 ribonuclease, on which there are two separate chapters The emphasis varies considerably from chapter to chapter in accordance with the known inclinations of the authors Thus Inagami writing on trypsin places the emphasis on enzymic mechanism, Hamaguchi and Hayashi strike a balance between enzymology and physical chemistry of egg lysozyme, the account by Tsugita and Ikeya-Ocada of phage lysozymes and λ endolysin contains a generous lacing of genetics, and the two chapters by Takahashi and by Oshima and Imahori on ribonuclease T_1 concentrate on the physical chemistry of the enzyme and its interactions Volume 2 has a rather curious assortment of subjects, directed, say the editors, towards mechanism and regulation of enzymes There are chapters on amylases, bromelain, the toxic protein, ricin, threonine deaminases, ribulose-1,5-diphosphate carboxylases and the significance of N-terminal acetylation The title has been cunningly chosen it is not "*The* Proteins", and it obviously does not compete in any sense with the set of volumes edited by Neurath "Some Proteins" might be an even better title, and it might well perhaps be regarded as a kind of supplement to the series of *Advances in Protein Chemistry*

A D'ALBIS

Illustrated Taxonomy

Classification of the Animal Kingdom An Illustrated Guide By R. B Freeman Pp 55 (English Universities London, 1973) £1 35

THIS admirable book, by one of the country's leading taxonomists, is a fully illustrated classification of the animal kingdom which deserves a wide circulation among sixth formers, first year biology students at universities, and interested amateurs including every young nephew, niece and cousin who shows a taste for natural history The classifications are authoritative, and the text is prefaced by an introduction on the principles and purposes of taxonomy The illustrations (by the staff of *Readers Digest*) are beautifully executed and sometimes rather touching· thus the illustration of *Dugong dugon* (the Dugong) has "evolutionary dead end" written all over its rather morose features.

P B MEDAWAR

Solar Environment

Coronal Expansion and Solar Wind By A J. Hundhausen Pp. xii+238 (Springer Berlin and New York, 1972.) 68 DM, \$21 60

THE decade elapsed since E. N Parker's monograph, *Interplanetary Dynamical Processes* (Wiley Interscience, New

York and London, 1963), has seen a flood of research into the solar-terrestrial environment. Accumulation of space observations, and of theoretical work stimulated by these data, has been increasingly demanding release through a new synthesis of the same ilk as Parker's. A. J. Hundhausen's new book satisfies this need in such a concise and lucid manner as to be equally suitable as an undergraduate text and as a research reference manual.

After a historical introduction, invaluable to non-specialists, Hundhausen classifies solar wind phenomena, identifying observed structures with characteristic theoretical time scales in the magnetized plasma. This provides a basis for the main themes of mathematical modelling of large scale phenomena in steady structureless flow of the wind and, subsequently, of non-steady flow in structured features.

Devotion of almost half the book to the steady flow problem itself indicates the "plethora of . . . partially proven theories" proposed to overcome the discrepancies between both one- and two-fluid wind models and observations. Though the author remarks, in typical style, that " . . . unique conclusions regarding the physical processes [which resolve this problem] . . . can be deduced only by true believers . . . ", he succeeds admirably in laying foundations for future work by sifting the morass of free parameters and coronal boundary conditions variously adopted in models.

Following a chapter on the role of helium and heavier elements in the steady wind, structure is introduced into the flow and it is at once evident that high speed plasma streams superposed on the quiet wind are the rule rather than the exception. The apparent transience of such streams is emphasized as due to the confinement of rapid plasma flow within magnetic sectors co-rotating with the Sun and their theoretical description is developed in this framework. Correlation of these stream sectors with the large scale organization of the solar magnetic field, rather than with active regions, appears as one of the most important results of spacecraft observations.

Severe transient solar wind disturbances in the form of flare-driven shocks provide the last theme and exemplify the improvement of data in the last decade—for example, a reduction from 100 to about 2 in the uncertainty factor in blast-wave mass estimates. Seeking to find some small fault in such an excellent book on a wide topic, one might consider incompleteness or typographical errors. Near total absence of the latter and coverage of omissions in a final bibliographic chapter, however, allow only an unqualified recommendation of the monograph.

JOHN C. BROWN

Nuclear Interactions

Fundamental Interactions and the Nucleus. By R. J. Blin-Stoyle. Pp. xv+345. (North-Holland: Amsterdam and London; American Elsevier: New York, 1973.) Dfl 60; $21.

FOR many years Professor Blin-Stoyle and his colleagues have made detailed studies of the manifestation of weak, electromagnetic and T-violating interactions in the nucleus. Now he has embodied the results of his studies in a comprehensive book that will be welcomed by all nuclear physicists.

After a short introductory chapter on fundamental interactions and the nucleus, the following four chapters (107 pages) are devoted to nuclear beta decay including a detailed consideration of the polar and axial vector currents, unusual hadron currents and interactions, and the lepton current and the neutrino. The next two chapters consider muon capture (27 pages) and the weak interaction potential (14 pages). The weak-interaction aspects of nuclear reactions follow, with chapters on the effect of a parity-violating potential in low energy processes, especially in alpha decay and in electromagnetic transitions (30 pages), and on time reversal invariance in nuclear reactions and in electromagnetic transitions (37 pages). Various electromagnetic and charge-dependent interactions are considered next (40 pages), with sections on the nuclear electromagnetic Hamiltonian, charge dependence of the inter-nucleon potential, magnetic dipole exchange effects and isospin multiplet energies, with a brief note on isospin in nuclear reactions. The last chapter is a very brief (8 pages) account of strong interactions in the nucleus. There are useful appendices on notation and conventions, relativistic and non-relativistic quantum mechanics, quantized fields, and isospin, charge symmetry and G-parity.

From this summary it will be clear that the scope of this book is much narrower than the title might indicate, and that it is concerned essentially with weak interactions and the nucleus, and even then there is no mention of electron scattering and muonic X-rays and the knowledge that can be obtained from them of the nuclear charge distribution. There is no account of the way the nuclear properties can be calculated from the nucleon–nucleon interaction or of kaon capture. The book is thus concerned essentially with the ways that various nuclear phenomena can be used to obtain more precise information about the fundamental weak nuclear interactions. As such, it is a very comprehensive and thorough review of a difficult field.

The need to make frequent use of field and group theoretical concepts and relativistic dynamics does not make for easy reading, and although it is impossible to develop these *ab initio* some more help could have been given to the less well-prepared reader by references to standard textbooks and review articles. Apart from this, the theoretical background is clearly described, with derivations of the formulae needed to interpret the experimental data.

Many of the most important investigations in this field, such as the determination of the parity-violating potential in nuclear reactions, the charge dependence of the internucleon potential and the detection of T-invariant second class currents in beta decay, require extremely precise experiments and very careful evaluation of all possible correction terms. Such work is comprehensively described with detailed and up-to-date references to the original work, and clear tables showing the present status of the problems. For this alone it will be invaluable to all research workers in the field.

There is a full list of references at the end. It would have been helpful to include an index of author and a fuller subject index.

P. E. HODGSON

Synthetic Method

Advanced Organic Synthesis. By Richard S. Monson. Pp. xii+203. (Academic: New York and London, June 1971.) $15; £7.

WRITING books on chemical synthesis seems to have become as popular (though hardly as rewarding) an occupation as actually working at it, with several recent examples ranging from analysis of strategy, through systematic listings of functional group transformations, to descriptive accounts of the nuts and bolts of the subject. Dr Monson's book fits firmly into the latter category. It contains detailed procedures for the preparation of 250 and more organic compounds, the vast majority of them being uncomplicated, one-step operations. In this respect the book is very similar in style to *Organic Synthesis*, though it cannot match the scope and detail achieved by fifty-two volumes of the latter. In fact, many of the procedures are taken directly from *Organic Synthesis*, to which the author has added a few general introductory remarks. The experiments are chosen so as to exemplify the following processes: oxidation, hydride and related reductions; dissolving metal reductions; hydroboration; catalytic hydrogenation, introduction of halogen; miscellaneous elimination, substitution and addition reactions; the Diels–Alder reaction; enamines; enolates, the Wittig reaction, reactions of trialkylboranes, carbenes; ethynylation, isomerization, carbon-carbon bond formation, and a few miscellaneous preparations including diazomethane and two peroxyacids, a few pages at the end are devoted to simple techniques such as distillation and adsorption chromatography.

This might seem to provide fairly wide coverage, with up to ten individual preparations under each heading, but there are a few serious omissions The experiments chosen reveal a preoccupation with alicyclic chemistry, there are far fewer examples from acyclic chemistry, only a few involving aromatic chemistry and hardly any from heterocyclic chemistry, nor are there any involving amino acids Several examples from these areas would have restored the balance which is lacking. A few more examples involving modern organometallic reagents are also called for In a few instances the procedure recommended is neither the most successful nor the simplest available For example, hydrolysis of the bromide on page 152 proceeds perfectly well in aqueous solution without adding silver nitrate, and the Wittig procedure on page 106 gives a poor yield of methylenecyclohexane It seems not to be widely known that replacement of the solvent ether by diglyme in this experiment improves the yield to almost the theoretical value. Generally, however, the book fulfils its purpose, which is to provide an introduction to organic synthesis for beginning graduate students and advanced undergraduates

M A McKERVEY

Day Length and Wobble

Rotation of the Earth. Edited by Paul Melchoir and Shigeru Yumi With the cooperation of Lady Jeffreys (International Astronomical Union/Union Astronomique Internationale Symposium No 48, held in Morioka, Japan, May 1971) Pp. xxii+244 (D Reidel Dordrecht, 1973.) Dfl 40

THIS book is based on papers given at the International Astronomical Symposium No 48, on the "Rotation of the Earth", held in Morioka, Japan, in May 1971 Attending were geophysicists and astronomers from North America, Europe and Japan, as well as several scientists from the USSR The book begins with a review by one of the editors, Dr P Melchoir, outlining the developments in the field since the publication in 1960 of Walter Munk and Gordon Macdonald's classic by the same title

Many of the papers were concerned with improvements in determining the Earth's polar motion (wobble) and changes in the length of day (ΔLOD) by optical observations of the "fixed stars" Several new sources of information on wobble and ΔLOD of the next decade, however, show potential for high accuracy These include observations of near-Earth geodetic satellites, lunar laser ranging experiments and the use of very long baseline interferometry In this respect, this volume provides invaluable references to the literature relating to these new developments

There are also several papers discussing how internal motions of the Earth, such as core–mantle interactions and continental drift, can be measured directly using these new techniques of fundamental astronomy Of special note is B D Tapley and B E Schultz's rigorous stochastic treatment of changes in the Earth's rotation, leading directly to models compatible with radar tracking data from near-Earth satellites The reader with a more speculative turn of mind will find satisfaction in learning of recent developments relating earthquakes, solar activity and observation of irregular changes in polar motion Earthquakes are also discussed as a source of excitation to the well known, but poorly understood, 14-month Chandler wobble

The proceedings of this conference, when combined with L Mansinha's collection of papers from a 1969 NATO Advanced Study Institute on *Earthquake Displacement Fields and the Rotation of the Earth* (D Reidel, Holland, 1970), make valuable references on progress since 1960 for workers in fundamental astronomy and geodynamics, and an important one for earth science, astronomical, and basic physics libraries

STEPHEN H PLAGEMANN

Radiomythology

Low-level Radiation By Ernest J Sternglass Pp xvi+166 (Earth Island London, February 1973) £2 50

IT must be presumed that Professor Sternglass never intended this book to be treated as a scientific work, otherwise he would not deliberately have misused scientific terms, used large numbers of very small units to give the impression of large quantities and been so highly selective in his use of the available data Instead he has written a popular account, a story, of the ideas which lead him to conclude that the deleterious effects of low-level radiation from nuclear fall-out have been grossly underestimated, particularly in respect to infant and foetal deaths Moreover, he claims that he was positively obstructed by the US Atomic Energy Agency and several leading scientists in presenting these ideas at the Congressional hearings on the effects of nuclear fall-out and in the scientific press

One reason for his hostile reception can be found in his claim that "the nature of modern science depends upon the free communication of even the most disturbing ideas, since only through their widest possible examination can the essential process of the gradual correction of errors be accomplished" If there were no more to it than this a few imaginative people could swiftly put an end to all scientific progress In this book Professor Sternglass has himself produced enough disturbing ideas to employ a whole army of scientists but he has not produced sufficient evidence to show that such effort would be rewarding It is not good enough merely for him to provide the ideas that certain specific increases in fall-out might have been the cause of certain specific adverse changes in the health of selected populations We need to know whether or not these ideas stand up to criticism when all the available data are considered, and, for example, if there is a relationship between foetal death and such diverse insults as a brief exposure to ^{131}I and the slow release of ^{90}Sr from maternal bone, what is the unifying factor and how it can be quantified in relation to risk

It is now a respectable hypothesis that all releases of radioactivity to the environment can be expected in the long term to increase the incidence of malignant disease and genetic mutations throughout the world All that is at issue is the magnitude of those increases and this is a matter which is under constant review by such reputable bodies as the United Nations Scientific Committee on the Effects of Atomic Radiation By presenting his claims now without a reasoned appraisal of the views of such bodies Professor Sternglass can only further alienate the support of many scientists who honestly seek to find the true relationship between risk and low-level radiation In this book he may have lost credibility even in the eyes of the most casual reader who, for example, will surely find it incredible that this man was actually waiting for the library doors to open in order to check that yet another trend in the US vital statistics supported his claims

There is a real need for the relevant facts to be put in simple terms before the public What a pity that Professor Sternglass, with his undoubted powers of popular expression, did not choose to present a more balanced view

J VENNART

Microbes Used by Man

Genetics of Industrial Microorganisms. Edited by Z. Vaněk, Z. Hošťálek and J. Cudlín. Volume 1: *Bacteria.* Pp. 496. Volume 2: *Actinomycetes and Fungi.* Pp. 511. (Elsevier: Amsterdam, London and New York, 1973.) Dfl. 225; $70.25.

THE chemical activities of microbes for centuries have been exploited to produce commercially useful chemicals and microbial cell material. From the beginning, improvements and developments were pragmatic, which is not surprising in view of the lack of any understanding of the biochemical activities of living cells, and the genetic control of these activities, until around the turn of the present century. The realization that conceivably just a minute part of the corporate microbial genome had been exploited for industrial purposes came only in the late 1940s and early 1950s with the discovery of a range of commercially useful antibiotics, and later the use of microbes in production of valuable steroid drugs. With the accompanying explosion in the growth of information about the biochemical and genetic activities of microbes, even the less imaginative among industrial microbiologists began to believe that microbes might, by appropriate biochemical and genetical manipulation, be made to yield an almost limitless number of commercially valuable chemicals. These in many ways were the sentiments which prompted some 600 scientists to convene in Prague in August 1970 at the First International Symposium on the Genetics of Industrial Microorganisms. The keynote of the symposium was eloquently expressed in the title which Professor A. L. Demain gave to his address "Marriage of Genetics and Industrial Microbiology—After a Long Engagement a Bright Future".

The proceedings of the symposium, in two volumes, have just been published—almost three years later. Such a long delay in publication must surely mean that at least some of the contributions are hopelessly out of date, especially since many of the participants to the symposium research in very active areas of molecular biology. The first volume deals with bacteria and the second with actinomycetes and fungi. Both volumes are well produced, which they should be with the swingeing price being charged for them. The first volume includes eight sections, dealing with genetics, mutagenesis, regulation of metabolism, and sporulation in bacteria. It also contains a most valuable section of four contributions on legal protection of strains, mutants, and genetic procedures, which includes accounts of problems which arise from litigation covering industrial microorganisms in Western (by W. L. Hayhurst) and Eastern Europe (A. Stoy), the importance of accurately describing producing organisms (H. B. Woodruff and his colleagues), and the problems of novelty in relation to litigation in industrial microbiology (Z. Řeháček). These contributions bring together information which is not readily accessible elsewhere, especially to the microbiologist, and is a most useful feature of the volume. The second volume of the proceedings is concerned principally with the genetics and metabolic regulation of streptomycetes and fungi, especially with the production of secondary metabolites such as antibiotics and alkaloids.

Nevertheless, the plain truth is that, over the past two decades, most of the major advances in industrial microbiology have still come from purely pragmatic approaches to problems of strain improvement, mainly through mutagenesis, and the refinement of cultural conditions. The contribution of genetics—the purposeful breeding of strains of industrial microorganisms with better performance characteristics—has been minimal indeed. This fact is reiterated, often with not a little coyness, in several of the contributions to these proceedings. Professor J. A. Roper, in an article on mitotic recombination and mitotic non-conformity in fungi, goes as far as to accuse the industrial microbiologist of a certain naiveté in believing that genetical manipulation could make a significant contribution to industrial microbiology. There have, undoubtedly, been technical barriers to the use of genetics in the microbiological industries, as well as biological barriers such as the possible existence of chromosome aberrations in highly mutated strains. Parasexual genetics has made some impact, especially in improving the quality of penicillin-producing fungi, but the contribution has been small, as Boyd Woodruff points out in his article in the second volume. Strangely, although the proceedings include a number of articles on metabolic control in yeast, there is no account of the role which genetical and biochemical research could make in improving brewing and baking strains of yeast. Here, surely, is an industrial microorganism which could be exploited genetically and biochemically; perhaps the brewers and the bakers are just not interested.

The contributions to these two volumes of proceedings contain a great deal of useful information on microbial genetics and biochemistry. Although they have been published far too late, these data are not to be found brought together elsewhere, and this in itself is sufficient recommendation to libraries to purchase the volumes. A second symposium on the Genetics of Industrial Microorganisms is to be held in Britain in 1974. Frankly, one cannot yet believe that the marriage to which Professor Demain referred has been consummated. Even now, might it not be possible for the organizers of the 1974 symposium to call it "Genetics and Industrial Microorganisms" rather than "Genetics of Industrial Microorganisms"?

ANTHONY H. ROSE

Biological Control

Principles of Biological Regulation: An Introduction to Feedback Systems. By Richard W. Jones. Pp. xiii+359. (Academic: New York and London, March 1973.) $16.

RICHARD JONES is no stranger to the problem of writing definitively about biological control systems. His earlier work in this field has largely been directed towards the reader with a firm grounding in engineering or physics. In this new book he has undertaken the much more difficult task of writing a book on the mathematical analysis of biological regulation, which is designed primarily for the life scientist.

The mathematical description of the principles of biological regulation is largely a question of organization. Historically, the understanding of homeostasis has progressed with each new insight into the organization of the organism from Bernard to Weiner and later workers. The continuation of this process inevitably leads to the use of mathematics.

The initial step in describing any biological system quantitatively is to organize the known facts in a block diagram or signal flow graph. In this book the author restricts himself primarily to the use of the block diagram with the simultaneous introduction of differential equations. The technique of developing each new mathematical idea in terms of a well known biological example is particularly useful, for it enables the reader, who is no doubt familiar with the qualitative description of the problem, to move more easily to a quantitative understanding.

Having introduced such concepts as transient response, and interacting and non-interacting processes, the author begins his discussion of feedback, which is the central principle of regulation. It is clear from block diagram algebra that any system which is to be analysed can be reduced to its canonical form, that is it can be reduced to one block in the forward pathway (efferent) and one block in the feedback pathway (afferent). In any discussion of regulation it is therefore logical to start from the canonical form.

This approach lends itself to the development of the open and closed loop gain equations and the concept of error. Within the book the understanding of these topics is rapidly reinforced by an appropriate examination of the operation of the thermoregulatory and blood pressure control systems

The quantitative description of a biological process is likely to require mathematics a little more complex than the simple algebraic equations associated with the canonical form This is particularly true when considering the dynamic response of a biological system Behaviour of this type is often investigated by methods such as Bode and Nyquist analysis, both of which are clearly described in the text However, immediately after this section of the text there is a brief introduction to the Fourier transform and its use in systems analysis In an introductory work of this type a two-page summary on the Fourier transform would seem inadequate, or indeed even inappropriate

Having described a repertoire of techniques, the author introduces the reader to their application in the analysis of human physiological systems Such a discussion inevitably results in the consideration of more advanced topics, such as the analysis of nonlinear and oscillatory systems These topics together with biochemical control form the material for the last two chapters Clearly, these are areas of great scientific importance, hence they should either be discussed in detail or omitted completely In view of the nature of this book, the latter course might be more appropriate

In summary, then, the aim of Richard Jones to write a book on the quantitative description of biological systems is entirely laudable In writing such a text the author is faced with the problem of steering a middle course between introducing mathematics which are beyond the scope of the reader but describe the biological situation accurately, or reducing the mathematical complexity to the point where the description is no longer realistic Nevertheless, in spite of the reservations noted, the result is a well balanced text which is certainly worth reading

R I KITNEY

Population Ecology

Populations in Seasonal Environment By S D Fretwell Pp xxiii+217 (Princeton University Princeton, New Jersey, January 1973) £5 75

THE first part of the preface and section 2 of this book are excellent The first part of the preface is a concise summary of the philosophy of science which is most welcome in a book of this sort Section 2, which is based largely on the author's own work with birds, provides an elegant example of scientific method, and would be worth reading for this alone The author has a flair for deduction, so elaboration of hypothesis into prediction is prominent in his work, and most elegantly done His explanations seem both original and profound as, for example, when his analysis of habitat selection in a territorial species suggests with simple inevitability that there must be selective advantage in the behaviour of both the winner and the loser in the territorial encounter This and other of Dr Fretwell's conclusions in this part of the book certainly have the generality that he himself modestly wished for them

Not so with section 1 The models are exclusively about populations in which there is no secular trend in density On page 5 the equation $d=\frac{b}{1+b}$ (which is fundamental to all the models) depends on the condition that $N=N(1+b)(1-d)$ And see page 3 "On the average the declines equal the gains so the population shows only random (*sic*) changes in size" This statement embodies a philosophical error that has long prevailed among a certain school of ecologists but it is disappointing to find it in one so perspicacious in philosophy as Dr Fretwell It is a philosophical error because it ignores time. It is palpably false on a geological time-scale on which any population may flower and most populations become extinct It is palpably false on the historical time-scale during the last 150 years in Australia many populations have flowered, and many others have greatly declined On the unrealistically short time-scale of the working life of an ecologist some populations seem to remain steady, but how can one test such a hypothesis without writing into the prediction some arbitrary short period of time, which makes the whole exercise trivial? Of course, Dr Fretwell is not interested in lack of secular trend *per se* but only as evidence for density dependence. But stability on a short time-scale is poor evidence for density dependence as the work of Den Boer and Reddingius has shown If Dr Fretwell had considered their work he may not have missed the obvious third contingency in discussing summer K and winter K

The logistic theory had a great vogue some five or six decades ago, but there were also some classical criticisms of it in the decades immediately following It was wrong to revive the theory without refuting the criticism of it To explain *Thrips imaginis* in terms of the logistic theory is nonsense because none of the assumptions is fulfilled

Section 1 may not be worth reading because it is trivial but section 2 is a must for all population ecologists especially those interested in birds

H G ANDREWARTHA

Colour Constancy

Surface Color Perception By Jacob Beck Pp xiv+206 (Cornell University Ithaca and London, February 1973) $11 50, £5 20

THIS book is concerned with the enormous gap that exists between the approach to colour by the physicist and by the artist The physicist or the physiologist starts with what is clear to him—the nature of the light coming to the eye from various objects, and the way that nerve signals are generated and modified, as can be recorded from the eye and the brain The artist or the psychologist starts from the other end with what is clear to him—perceptions of the colour and the lightness of the objects themselves

The author evidently sees that the psychological complexity with which he has to deal is well beyond the reach of today's electrophysiology, and therefore ignores the known way that nerve signals are generated and processed and received in various parts of the brain Instead, his treatment is to speculate upon the way that one aspect of perception may interact with others to account for what subjects say they see, in a very large variety of experimental situations

The central problem is the famous and ancient question of colour constancy—how we manage to name the colour and lightness of objects around us "correctly", even when the colour and brightness of the illumination are changed so that the light entering the eye becomes quite different

This is exceedingly hard to explain, especially since what is perceived is strongly influenced by what is expected One kind of organization considered is expressed as follows "Whether the stimulus is seen as a white in reduced illumination, or as a grey, depends upon whether the stimulus cues and an observer's attitude induce the perceptual system to assimilate the sensory signals to a schema of a white plus a correction for the reduced illumination, or a schema for a grey surface normally illuminated" This and alternative formulations may help psychologists to form some idea of what goes on in the mind to correct (or misrepresent) the primary sensation in a wide range of carefully examined conditions

Indeed the importance and value of the book lie in the thorough way in which the very many aspects of surface colour are treated, the great number of classified experiments that are briefly described (with references), and the enumeration with contrast of interpretations advanced by various authorities

The book is beautifully produced, and colour-plate 1 is a fascinating illustration of the variety seen in object colours. W A H RUSHTON

CORRESPONDENCE

Infant Precocity

SIR,—Leiderman *et al* reported[1] that social factors made an important contribution to precocity in African infants We have found that Arab infants in Lebanon are also precocious

In a study of mental development throughout the course of rehabilitation of severely malnourished infants[2] we also tested a group of thirty healthy infants of the same low socio-economic class, matched for age and sex, all growing well by an Index of Thriving[3] The average monthly income of the family was only about US $90 with four or five children per family, most of the mothers illiterate and a few fathers with primary education Each child was tested at 2-week intervals by a bilingual Arab female psychologist using the Griffiths Mental Development Scale This test has five functions, locomotor, personal-social, hearing and speech, eye-hand coordination and performance, the expected United Kingdom score being 100 A total of seventeen infants were tested for the maximal number of eight consecutive sessions and a follow-up test about 4 months later The mean values and standard deviations are shown in Table 1 It will be seen that without exception the mean value was over 100 and frequently well above this The score tended to be highest for locomotor function and lowest for hearing and speech (the area most affected by malnutrition) Sixteen children from among the original thirty were tested by the Stanford Binet Intelligence Test nearly 4 yr later when they were still growing well, as part of a study of the long-term effects of malnutrition on mental development[4] The mean (±s d) IQ then was 98 7 (±7 1) with no precocity

Yours faithfully,

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Table 1 Mean (±s d) Values for Seventeen Lebanese Infants on Griffiths Mental Development Scale

Test	Age (weeks)	Mental age	Developmental quotient	Locomotor	Personal-social	Hearing and speech	Eye-hand coordination	Performance
1st	26 7	29 5	109	111	112	103	110	108
s d	11 3	12 0	8 4	15 4	11 6	10 6	14 7	9 9
2nd	28 0	33 5	112	115	115	111	111	107
s d	11 5	14 1	10 6	19 3	9 2	11 6	7 8	15 9
3rd	30 3	34 3	117	114	115	111	108	107
s d	11 7	13 5	6 9	13 4	8 1	8 7	8 7	13 5
4th	32 8	35 3	109	114	112	107	109	103
s d	11 5	13 7	11 2	14 4	13 8	10 1	13 9	14 2
5th	34 2	38 8	112	116	115	108	109	110
s d	11 6	12 6	7 0	12 5	7.5	9 3	9 0	11 2
6th	36 2	40 9	111	117	114	104	105	111
s d	11 5	11 3	6 9	13 9	9 5	9 8	9 0	8 1
7th	38 2	43 2	113	115	114	106	109	112
s d	11 5	11 1	8 1	15 2	9 3	9 9	11 3	8 2
8th	40 5	44 5	111	115	113	105	110	109
s d	11 4	10 6	7 5	11 8	6 5	8 0	10 7	10 9
Follow-up	57 6	61 4	108	116	109	102	110	106
s d	12 9	11 4	10 4	10 4	8 4	10 4	10 9	10 4

Grassy but not Graminae

SIR,—I should like to correct a misconception which appeared in *Nature*, **243**, 342 (1973) In "Grass Roots at the Base of the Neogene", M D Brasier comments on the likely ecological effects of "marine grasses" when these first invaded reef communities He says, "It follows that remarkable changes must have occurred after the initial colonization of the seafloor by the Gramineae" Unfortunately, although the name "seagrass" is commonly used to refer to marine angiosperms in general, they are not true grasses (members of the family Graminae) They represent a variety of groups within the monocotyledons[1] *Thalassia*, the one genus named is, for example, a member of the family Hydrocharitaceae[2] The name "seagrass" comes from the generally linear or strap-shaped leaves of these marine flowering plants, which are superficially like the leaves of many grasses

Yours faithfully,

P B TOMLINSON

Maria Moors Cabot Foundation for
Botanical Research,
Harvard University

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Austin, Texas 78712
"An Equal Opportunity Employer"

(475)

AUSTRALIAN NATIONAL UNIVERSITY

Applications are invited for the following

RESEARCH SCHOOL OF PHYSICAL SCIENCES

POST IN THEORETICAL PHYSICS Appointment will be at the level of **Senior Fellow, Fellow, Senior Research Fellow** or **Research Fellow** in the Department of Theoretical Physics which at present has an academic staff of fifteen, headed by Professor K J le Couteur, F A A Preference for this appointment will be given to applicants interested in theoretical aspects of solid state physics or nuclear physics The Department also has research interests in the general field of statistical mechanics and elementary particle physics Closing date October 12, 1973

RESEARCH SCHOOL OF PACIFIC STUDIES

POSTDOCTORAL FELLOWS . Applications will be considered from persons qualified in any of the following fields, for appointment as Postdoctoral Fellows in the Research School of Pacific Studies

Anthropology , Biogeography and Geomorphology (including Quaternary palynology) , Economics , Far Eastern History , Human Geography , International Relations , Linguistics , Pacific History (including Southeast Asian History) , Prehistory

Postdoctoral Fellowships are intended to attract young scholars who have just recently qualified and have an immediate research interest that can be pursued with special advantage in the Research School of Pacific Studies Applicants should if possible give an outline of the topic or topics they would like to work on while holding a Postdoctoral Fellwship Successful applicants should preferably be able to commence duty by early 1974 Cosing date September 21, 1973

RESEARCH SCHOOL OF CHEMISTRY

FELLOW or SENIOR FELLOW The School proposes to make not more than two appointments at the level of **Fellow** or **Senior Fellow** in the following research areas

Physical organic chemistry, preferably but not exclusively in quantitative investigations of mechanisms,
Synthetic organic photochemistry ,
Synthetic organic electrochemistry

The appointments would be connected with the organic work of the school at present conducted by Professor A J Birch Mr R W Rickards and Dr J K MacLeod The School is non-departmental, and opportunities exist for co-operation with other groups in the School The appointees would principally conduct independent research, with some support by postdoctoral workers and Ph D students, and would be expected to assist with other aspects of postgraduate training and school administration Closing date September 28, 1973

POSTDOCTORAL FELLOWS or RESEARCH FELLOWS Applications are invited for appointment in 1974 to a number of Postdoctoral Fellowships or Research Fellowships It is intended that appointments will be made for work with the members of staff whose names are indicated in the following groups

Organic Chemistry (Professor A J Birch, Mr R W Rickards) Structure determination and biosynthesis of natural products, including antibiotics and other biologically-active compounds, mould metabolites, and plant and marine products , insect chemistry , total synthesis involving new reactions , organic aspects of organometallic chemistry

Inorganic Chemistry (Professor R L Martin Dr A M Sargeson, Dr D A Buckingham) Synthesis, structures, and reactions of new ligands and their transition metal complexes (with the present emphasis being centred on sulphur and selenium based chelating ligands) magnetochemistry, especially the study of metal-metal interactions in paramagnetic clusters stereochemistry, synthesis, structures and mechanisms of substitution and reactions at co-ordinated ligands Current interests are centred on mechanisms of ester, amide, nitrile, phosphate ester and olefin hydrolyses , stereospecific synthesis of organic molecules using inorganic complexes strategy in the synthesis of chelate complexes inorganic biochemistry of Fe, V, Cr, Co and calculations of structures of minimum energy

Physical Chemistry (Professor D P Craig, Dr J Ferguson) Electronic Spectroscopy, especially of crystalline solids U V spectroscopy and photochemistry especially of molecular crystals and small aggregates Transition metal ion spectroscopy, ion pair interactions, exchange effects and magnetic circular dichroism

Theoretical Chemistry (Professor D P Craig) Intermolecular forces Electronic properties of molecular crystals Closing date September 28, 1973

Since the School, by reason of its non-departmental structure, affords opportunities for collaboration with members of staff working in other areas, details follow of research activities in areas in which at present there are no vacancies

Organic Chemistry · (Dr J K MacLeod) Mass spectrometry including deuterium-labelling studies of specific fragmentation processes , combined g c -m s analyses of biological mixtures

Inorganic Chemistry (Dr M A Bennett) Synthesis, stereochemistry and reactions of organometallic complexes, with emphasis at present on metal-olefin, tertiary phosphine and carbonyl complexes, and on the stabilisation of small ring acetylenes on metals

X-Ray Crystallography (Dr G B Robertson) Structural Chemistry of organometallic, inorganic and biologically active organic molecules (with present emphasis on organometallics) Improved methods in X-Ray diffraction analysis

Physical Chemistry (Dr R Bramley) Electron spin resonance spectroscopy, particularly of photo-excited triplets in molecular crystals Nuclear magnetic resonance spectroscopy

Chemistry in Non-Aqueous Solvents · (Dr A J Parker) Postdoctoral and Research Fellows will continue to work in the following areas during 1974, after the group leader, Dr A J Parker, takes up his chair at Murdoch University, W A solvent effects on rates, equilibria and mechanism of organic and inorganic reactions Cuprous chemistry, calorimetry, hydrometallurgy and electrochemistry

Analytical Chemistry (Miss B J Stevenson) Micro and submicro metal and anion analyses

RESEARCH SCHOOL OF BIOLOGICAL SCIENCES

POSTDOCTORAL FELLOW—PHOTORECEPTOR—MEMBRANES Appointment will be in the Department of Developmental Biology (Head Professor D J Carr) The successful applicant will be expected to contribute to a programme examining the interaction of the protein, phytochrome, with cellular membranes Phytochrome is a plant photoreceptor recently shown to mediate light-induced changes in the properties of a particulate fraction with which it is associated Applications will be considered from candidates with experience in one or more of the following areas membrane biochemistry and/or biophysics , allosterism , phytochrome isolation and characterisation , molecular photobiology Closing date September 28, 1973

RESEARCH SCHOOL OF EARTH SCIENCES

RESEARCH FELLOW The Research School of Earth Sciences has an academic staff of 21 headed by Professor A L Hales The Fields of interest of the School include Experimental Petrology and Geochemistry, Isotope and Trace Element Geochemistry Rock Mechanics, Rock Magnetism, Terrestrial Magnetism, Heat Flow and Seismology Applications will be considered from persons with interests in either of the two following fields

Seismology—Applicants should have some knowledge of seismic data processing and field studies of crustal and upper mantle structure

Mass spectrometry—Applicants should be experienced in the ion optics of mass spectrometer design and in applications of mass spectrometry to isotope geochemistry Closing date October 5, 1973

SALARIES Salary on appointment will be in accordance with qualifications and experience within the ranges Senior Fellow $A14,308-$A16,462 per annum (6×359) Fellow $A10,432-$A14,288 per annum (5×428 , 4×429) Senior Research Fellow $A12,778-$A15,116 per annum (3×390 , 2×389 1×390) Research Fellow $A8,698-$A11,901 per annum (2×641 , 2×640 , 1×641) , Postdoctoral Fellow $A8,698-$A11,901 per annum Current exchange rates are approximately $A1 55p $US1 41

OTHER CONDITIONS : Tenure of appointment as Senior Fellow and Fellow is for five years in the first instance with the possibility of extension to retiring age , Senior Research Fellow and Research Fellow normally for three years in the first instance with the possibility of extension to a maximum of five years , Postdoctoral Fellow for not less than one year and not more than two years (two years for overseas appointees) Postdoctoral Fellows would normally have recently completed the Ph D degree

Reasonable travel expenses are paid and assistance with housing is provided for an appointee from outside Canberra Superannuation (where applicable) is on the FSSU pattern with supplementary benefits

The University reserves the right not to make an appointment or to make an appointment by invitation at any time

Further information should be obtained from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (484)

INSTITUTE OF CONNECTED EDUCATION

offer prizes for research in pure general science That is, research in interdisciplinary sciences, or if and how all sciences are interconnected Main object of the Institute is to create and sponsor the acceptance of a course of this nature in schools, colleges and institutes

For further information please apply in writing to **The Secretary, Institute of Connected Education, 28a Cadogan Place, London SW1X 9RX.**

(538)

Cardiff Royal Infirmary

Newport Road, Cardiff

Basic Grade Biochemist

required in the newly established National Protein Reference Unit (Department of Chemical Pathology) This appointment will be for one year in the first instance, with an option to renew

Applicants must hold an appropriate science degree and should have experience of routine chemical pathology with a special interest in vitamins The successful candidate will be expected to collaborate in research and development in addition to the service commitment

Salary scale £1,278 per annum rising to £2,370 per annum (Candidates with 1st or 2nd Class Honours commence at £1,566 per annum, and it is possible to award a higher starting point in the light of postgraduate study) Whitley Council conditions of service apply

Further particulars may be obtained from *Dr J W Keyser, Institute of Pathology*, at the above hospital, who will be pleased to arrange for a visit to the Department

Application form from the Personnel Department at the hospital

(472)

LAKEHEAD UNIVERSITY

Faculty of Science

A RESEARCH ASSOCIATE

is required for one year to join a small group working on heterogeneous catalysis and surface chemistry Preference will be given to candidates with post-graduate experience in one of these areas

Applications, including the names of three referees, should be sent to R A Ross, Dean, Faculty of Science, Lakehead University, Thunder Bay, Ontario, Canada P7B 5E1 (471)

UNITED BRISTOL HOSPITALS

SENIOR BIOCHEMIST

Applications are invited for the post of Senior Biochemist to work in the new laboratories of the Bristol Royal Infirmary The duties will include the introduction of analytical techniques, particularly in relation to the monitoring of drug levels in the blood Salary scale £2,613-£3,375

Applications with the names of two referees to Dr G K McGowan, Department of Chemical Pathology, Royal Infirmary, Bristol BS2 8HW, not later than September 21, 1973 (467)

NORTH EAST LONDON POLYTECHNIC

DEPARTMENT OF PHYSICS

RESEARCH ASSISTANT

Applications are invited from good honours graduates to commence as soon as possible work on the investigation of surfaces under UHV conditions using the techniques of Auger spectroscopy, Ellipsometry and LEED The appointment will be for two years initially with possible extension for a third year

Salary scale £1,320 per annum with annual increments of £55 to £1,485

Please request application form of The Academic Staffing Officer, Ref S/CF 221, North East London Polytechnic Forest Road London E17 4JB Tel 01-527 2272, for return by September 10, 1973

(458)

UNIVERSITY OF QUEENSLAND

AUSTRALIA

SENIOR TUTOR IN BIOCHEMISTRY

(Two positions)

Minimum qualifications Honours degree in Science but higher degree preferred Successful applicant expected to assist with the organization of practical classes at both second and third year level, to give a number of lectures and to participate in departmental research programme

Salary $A7,270 to $8,698 per annum

Other Benefits Superannuation similar to F S S U , housing assistance, and travelling and removal expenses

Additional information and application forms are obtainable from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

Applications close in London and in Brisbane on **5 October 1973** (510)

LABORATORY TECHNICIAN

with biochemical experience required to join a team working on a long term grant from the MRC to study cell separation techniques and steroid biosynthesis Qualifications Associate of IMLT or equivalent Experience in animal work and general administration an advantage Salary on Whitley Council scales according to qualifications and experience , minimum £1,461 per annum including London weighting

Apply, with the names of 2 referees, to The Secretary (N), Department of Physics as Applied to Medicine, The Middlesex Hospital Medical School, London W1P 6DB (463)

UNIVERSITY OF WALES

THE WELSH NATIONAL SCHOOL OF MEDICINE

DEPARTMENT OF HAEMATOLOGY

SCIENTIFIC OFFICER

A BIOCHEMIST with experience in protein synthesis is required to join a unit studying the characterization and synthesis of iron containing proteins by mammalian cells Salary will be in the range £1,566-£2,370 per annum or £2,613-£3,375 according to age, qualifications and experience

Further details available from the Registrar, The Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN (460)

UNIVERSITY OF TASMANIA

LECTURESHIP IN GEOLOGY

Applications are invited for the above-mentioned post Appointment will be offered in one of the following scales, according to qualifications and experience

Lecturer Grade II $A8,698—470×1—469×2—$A10,106 ,

Lecturer Grade I $A10,575—469×3—$A11,982,

and will be made in one of the fields of exploration geophysics or economic geology or structural/metamorphic geology

Application forms and further particulars are available from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

Applications close on September 19, 1973 (461)

UNIVERSITY OF LEEDS

DEPARTMENT OF BIOCHEMISTRY

Applications are invited for the post of TECHNICIAN grade 3 to assist in a programme of research into mammalian protein synthesis Applicants should be experienced in general biochemical laboratory techniques of chromatography, radioactive counting, etc Salary £1,539-£1,794 a year

Applications in writing, stating age, qualifications and experience, to The Secretary, Department of Biochemistry, 9 Hyde Terrace, Leeds LS2 9LS (478)

UNIVERSITY OF SHEFFIELD

DEPARTMENT OF INORGANIC CHEMISTRY

CASE AWARD IN ORGANOMETALLIC CHEMISTRY/CATALYSIS

Immediate applications are invited for a CASE Award under the joint supervision of Professor P M Maitlis and Dr C White (University of Sheffield) and Professor R C Pitkethly (British Petroleum Company)

The project will involve the preparation and study of both new homogeneous and new supported metal catalysts, of industrial interest, capable of promoting hydrogenation in the presence of sulphur-containing compounds and the hydrogenation of polycyclic aromatic hydrocarbons The work will be carried out using the facilities both at Sheffield and at the B P Research Laboratories in Sunbury

The successful candidate should possess a good honours degree (or equivalent qualification) and will be expected to register for the degree of Ph D

Applications, consisting of a curriculum vitae and the names of two referees, should be sent to Professor P M Maitlis Department of Chemistry, The University, Sheffield S3 7HF Quote Ref R 66/G (456)

UNIVERSITY OF HONG KONG

LECTURESHIP/ASSISTANT LECTURESHIP IN MECHANICAL ENGINEERING

Applications are invited for the above-mentioned post Applicants should have some years of experience in industry Preference will be given to persons with expertise in detailed mechanical design

Annual salaries (superannuable) are

Lecturer HK$40,800×2,760—46,320 BAR 49,080×2,760—68,400 ,

Assistant Lecturer HK$29,760×2,760—38,040

At the time of issue the rate of exchange is £1=HK$12 80 approx

Starting salary will depend on qualifications and experience Salaries for female appointees below HK$62 880 are slightly lower than given above , equalization of male and female salary scales will be achieved by April 1, 1975

Further particulars and application forms may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF, or the Secretary to the Council, University of Hong Kong

Closing date for applications is September 15, 1973

(464)

Glaxo

Assistant Librarian

Stoke Poges, Bucks.

This vacancy has arisen at our Sefton Park, Stoke Poges Laboratories The person appointed will report direct to the Librarian in charge of a small group giving a comprehensive service to three research departments

He or she will be required to scan incoming literature, undertake literature searches and compile bibliographies, answer general and technical enquiries and classify additions to the library A knowledge of foreign languages would be an advantage

Ideally, candidates will have reached degree standard, preferably in a natural science subject and will be Associates of the Library Association The position offers an excellent opportunity for varied and interesting work, and an attractive salary will be offered to secure the right person

Other benefits include contributory pension, profit sharing bonus and catering and sports club facilities

Please write giving brief details and quoting ref U 597 to the Senior Personnel Officer (Research), Glaxo Laboratories Limited, Greenford, Middx UB6 0HE

(515)

WELSH PLANT BREEDING STATION UNIVERSITY COLLEGE OF WALES

Applications are invited for a SCIENTIFIC OFFICER Grade post on the Staff of the Station

The Officer appointed will assist in the conduct of breeding programme based on the utilization of haploids for the production of disease resistant varieties of spring barley

Candidates should hold a University Pass Degree or National Certificate in an appropriate field

Salary scale £1,318 to £2,177 maximum per annum

Letters of application, together with the names of two referees, should be sent to the Secretary, Welsh Plant Breeding Station, Plas Gogerddan, Nr Aberystwyth SY23 3EB, on or before September 30, 1973 (494)

THE WEST OF SCOTLAND AGRICULTURAL COLLEGE

DEPARTMENT OF MICROBIOLOGY

RESEARCH ASSISTANT

Applications are invited for the above post from candidates holding an Honours degree in Microbiology or Bacteriology with a sound basis of Biochemistry and preferably an interest in pollution control The officer will join a group investigating the treatment and utilization of animal wastes

Salary (dependent on age, qualifications and experience) will be on Grade IV—£1,402 (Honours Graduates £1,499) rising to £1,925

Application forms and conditions of appointment are obtainable from the Secretary, The West of Scotland Agricultural College, Auchincruive, Ayr KA6 5HW, with whom applications should be lodged by September 14, 1973 (495)

HAMPSHIRE COUNTRYSIDE INFORMATION OFFICER

£1,803-£2 388

A new appointment in the County Land Agent & Valuer's Department to develop the information and interpretation services for rapidly expanding countryside projects in Hampshire Responsibility for creating and implementing interpretive programmes, to include lectures, guided walks, displays, and publication of nature trail leaflets

He or she must have a broad knowledge of natural history, archaeology and history, coupled with enthusiasm and the ability to communicate with all types of people

Further particulars and application forms (returnable by September 24) may be obtained from the Clerk of the County Council, The Castle, Winchester Please quote ref SE1893 U (Preference will be given to Local Government Applicants) (465)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTFORDSHIRE AL5 2JQ

SCIENTIFIC OFFICER for Biochemistry Department to assist in enzymological work in relation to nitrogen metabolism in plants The appointee will be expected to take some responsibility for specialized equipment in the department Applicants should hold a degree, H N C or equivalent qualification in some area of biology or chemistry, and have a special interest in biochemistry Preference may be given to candidates with previous experience in a research laboratory, but recently qualified applicants will be considered Starting salary £1,318 to £1,590 (depending on qualification and experience) on scale to £2,177 Superannuation

Applications, naming two referees and quoting Ref 1982, to the Secretary by September 21, 1973 (520)

GRADUATE SECRETARY

required for a Director of a Pharmaceutical Research and Manufacturing Company Applicants must have good typing speeds preferably with Dictaphone experience and should have attained a degree in a Biological Science subject The work is varied and the position progressive Application forms from the Secretary, Biorex Laboratories Limited, Biorex House, Canonbury Villas, London N1 2HB (486)

UNIVERSITY OF LONDON

GRANTS FOR RESEARCH

Applications are invited from members of the University and teachers in School of the University for grants from the Central Research Fund to assist specific projects of research and for the provision of special materials and apparatus Grants are not made for normal maintenance

Applications must next be received not later than September 15 Forms of application and further particulars may be obtained from the Secretary to the Central Research Fund University of London, Senate House, London WC1E 7HU (496)

UNIVERSITY OF LONDON INSTITUTE OF PSYCHIATRY

DEPARTMENT OF BIOCHEMISTRY

Applications are invited for the post of RESEARCH WORKER, Research Council supported, from November, 1973, until June, 1975, for investigation of simple purine derivatives in neurohumoral processes in the brain Salary including London Allowance, within the range £1,773 to £2,550 per annum, according to qualifications Ph D in Biochemistry preferred Eligible for F S S U

Further details and application form from the Secretary, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, quoting reference HM/N (497)

UNIVERSITY OF RHODESIA

FACULTY OF MEDICINE

LECTURESHIP IN PHARMACOLOGY

Applications are invited for the post of Lecturer in Pharmacology at the Godfrey Huggins School of Medicine with effect from January 1, 1974 The successful applicant will be required to teach students enrolled for the MB, ChB, Honours BSc in Pharmacology, and BPharm Degree courses Applicants should be in possession of a medical degree or a qualification in Pharmacology Good facilities exist for research in biochemical pharmacology/drug metabolism

Salary scales (approx sterling equivalent)

Medically qualified

Senior Lecturer	£6,002×£181—£7,450
Lecturer Grade I	£5,562×£155—£6,182
Lecturer Grade II	£4,690×£155—£5,620

Non-Medically qualified

Senior Lecturer	£4,707×£181—£6,155
Lecturer Grade I	£4,266×£155—£4,886
Lecturer Grade II	£2,634×£129—£3,021×£155—£4,106

(Medically qualified members of staff who have served for at least three years on the maximum of the Senior Lecturer's scale may be considered for a special additional increment)

Family passages and allowance for transport of effects on appointment Installation loan of up to half of one year's salary if required Unfurnished University accommodation guaranteed for a period of three years for persons recruited from outside Rhodesia Sabbatical and triennial contact visits with travel allowance Superannuation and medical aid schemes

Detailed applications (six copies), giving full personal particulars (including full names, place and date of birth etc), qualifications, experience and publications, and naming three referees, should be submitted by September 30, 1973, to the Senior Assistant Registrar, Godfrey Huggins School of Medicine, University of Rhodesia, P O Box MP 167, Mount Pleasant, Salisbury, Rhodesia, from whom further particulars may be obtained When applying please quote Ref No UK/19/73 and state where advertisement seen An additional copy of application should be sent to the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF (462)

CHAIRMAN AND SENIOR SCHOLAR, DEPARTMENT OF KINESIOLOGY Administer innovative undergraduate and graduate programmes comprising 500 students/25 faculty Candidates should submit vitae including research record in scientific aspects of human physical activity in either bio, bio-physical or behavioural sciences by November 1, 1973 to Gerald S Kenyon, Dean, Faculty of Human Kinetics and Leisure Studies, University of Waterloo Waterloo, Ontario, Canada (476)

SCOTTISH PLANT BREEDING STATION

Higher Scientific

or

Scientific Officers

Applications are invited for two vacancies in the Potato Department at the Scottish Plant Breeding Station

Post (a)

An officer is required to improve and develop screening techniques for assessing the disease resistance of clones passing through the general breeding programme and to carry out research into host/parasite relationships

A background of mycology or plant pathology would be most appropriate although candidates with more general training in Botany or Plant Science should apply

Qualifications: First or upper Second Class Honours degree in a biological subject

Salary· Scientific Officer scale (£1,590 to £2,177 per annum) Higher Scientific Officer scale (£2,076 to £2,667 per annum) depending on experience

Superannuation under F S S U with compensatory non-pensionable allowance of 4½% of gross salary to offset contributions

Post (b)

An officer is required to assist and to become familiar with the work proceeding on potato virus diseases in relation to the potato breeding programme and to assume limited responsibility for the conduct of a part of the work A background in genetics or virology would be most appropriate though interested candidates from other biological specializations should apply

Qualifications· HNC, pass degree or equivalent either in a biological subject or with other appropriate experience

Salary Scientific Officer scale (£1,318 to £2,177 per annum) or Higher Scientific Officer scale (£2,076 to £2,667 per annum) depending on qualifications and experience, a minimum of 5 years' post-qualifying experience being required for appointment to the higher grade

The post is superannuated with contributions offset by a non-pensionable allowance of 5½% of gross salary

Application forms and further information from the Secretary, Scottish Plant Breeding Station, Pentlandfield, Roslin, Midlothian EH25 9RT, to be returned not later than September 29, 1973

Applicants from the Agricultural Research Service should submit their application through their present Directors if they wish to be considered for the award of "public interest" transfer terms

(504)

IMPERIAL COLLEGE

Department of Zoology and Applied Entomology Systems Analysis in Resource Management

ASSISTANT RESEARCH OFFICER

required in The Environmental Resource Management Research Unit which was established in 1970 under a grant from The Ford Foundation Duties will involve assisting in research on the modelling of pest populations and other resource problems, and will involve statistical analysis and computer programming Candidates should be mathematics or biology graduates and have had training in computer programming and statistics The successful candidate will be expected to work at Imperial College Field Station Ascot, Berks, where there is a terminal to The University of London's CDC 6600 computer Commencing salary in range £1,545 to £1,992 depending on qualifications and experience, plus F S S U benefits

Applications (two copies), naming two referees, should be sent to Professor T R E Southwood, Imperial College Field Station Silwood Park, Ascot, Berks, before September 15 (501)

YORK UNIVERSITY

Toronto, Canada

CENTRE FOR RESEARCH IN EXPERIMENTAL SPACE SCIENCE

POSTDOCTORAL PROJECT SCIENTIST

FOR RADIATIVE TRANSFER STUDIES IN MOLECULAR ATMOSPHERES

Applications are invited for a postdoctoral project scientist position for work on radiative transfer in molecular atmospheres using computer-oriented synthetic spectral methods Candidates should have a good knowledge of molecular spectroscopy and radiative transfer theory and be experienced in programming and the use of computers

Applicants should send a curriculum vitae and the names and addresses of at least two referees to Professor R W Nicholls, Director, Centre for Research in Experimental Space Science, York University, 4700 Keele St, Downsview, Ontario M3J 1P3, Canada, from whom more information may be obtained (488)

UNIVERSITY OF LEEDS

DEPARTMENT OF BIOCHEMISTRY

Applications are invited for the post of JUNIOR TECHNICIAN to assist in the servicing of teaching laboratories for science and medical students The successful applicant will undergo further training with day release, and will be a member of a team of technicians under the direction of a senior person Salary, £717-£1,155 a year

Applications in writing, stating age, qualifications and experience, to The Secretary, Department of Biochemistry, 9 Hyde Terrace, Leeds LS2 9LS (479)

UMIST

RESEARCH TECHNICIAN

(REF BIO/385/AI)

Applications are invited from candidates with suitable qualifications and experience to work as Grade 3 Technician on a SRC project of 3 years duration concerned with pyruvate carboxylase in thermophiles

Starting salary £1,539 per annum

5-day week, 4 weeks annual leave and Superannuation Scheme

Requests for application forms, quoting reference number, should be sent to the Registrar, U M I S T, Sackville Street, Manchester M60 1QD Closing date for applications September 14, 1973 (480)

ROYAL POSTGRADUATE MEDICAL SCHOOL

STUDENT/JUNIOR TECHNICIAN

required in the Department of Immunology Post suitable for School leaver holding a minimum of GCE 'O' level passes in English, Mathematics and two Science subjects Salary in the range £762 to £1,416 per annum according to age and experience Day release for further studies will be given

Applications to Secretary, Royal Postgraduate Medical School Hammersmith Hospital, Du Cane Road London W12 0HS, quoting reference 21/203/N (477)

UNIVERSITY OF OTAGO

DUNEDIN, NEW ZEALAND

LECTURER OR SENIOR LECTURER IN BIOCHEMISTRY

Applications are invited, particularly from young graduates with postdoctoral experience, for the position of Lecturer or Senior Lecturer in Biochemistry.

Preference will be given to candidates whose research interests lie in the field of mammalian metabolism and its control but well-qualified applicants in other fields of biochemistry will be considered

Salary scales Lecturer $NZ5,862-$7,497 per annum, Senior Lecturer $NZ7,633-$9,813 per annum with a bar at $8,997 per annum

Salary scales are subject to both triennial review and cost-of-living adjustments

Further particulars are available from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square London WC1H 0PF, or from the Registrar of the University

Applications close in New Zealand and London on September 30, 1973 (487)

UNIVERSITY OF READING

LECTURESHIP IN ZOOLOGY

Applications are invited for a Lectureship in Zoology from candidates with interests in freshwater biology and/or fisheries

The person appointed should take up duties on January 1, 1974, or such other date as may be arranged

Further particulars may be obtained from the Registrar (Room 208, Whiteknights House), The University, Whiteknights, Reading RG6 2AH, by whom applications should be received not later than September 29, 1973 (482)

UNIVERSITY OF OTAGO

DUNEDIN, NEW ZEALAND

APPOINTMENT IN MATHEMATICS

Applications are invited for appointmentt as LECTURER in the Department of Mathematics Applications will be considered from candidates with qualifications in analysis

Salary scale $NZ5,589 to $7,149 per annum Salary scales are subject to both triennial review and regular cost-of-living adjustments

Further particulars are available from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF, or from the Registrar of the University

Applications close in New Zealand and London on **October 15, 1973** (523)

GLASSHOUSE CROPS RESEARCH INSTITUTE

SCIENTIFIC OFFICER

Required in Entomology Department to work as member of team developing integrated programmes for control of crop pests Applicants should be over 21 and possess degree, H N C or equivalent qualification in Entomology or Zoology Salary within scale £1,318 to £2,177 according to qualifications and experience Contributory superannuation scheme

Further particulars obtainable from Secretary of Institute, Worthing Road, Rustington Littlehampton, Sussex, to whom applications should be sent by September 28, giving full biographical details and names and addresses of two referees (506)

THE UNIVERSITY OF HULL

DEPARTMENT OF PHYSICS

A TECHNICIAN (Grade 4) is required for maintenance of equipment and facilities in undergraduate teaching laboratories, supervision of lecture theatres, and organization of lecture demonstration experiments Salary on scale £1,728 to £2,028 per annum Applicants should have a wide knowledge of physics measurement techniques and instrument maintenance, and a knowledge of electronics Applications, citing the names of two scientific referees, to the Technical Staff Officer, University of Hull, by September 12 quoting Ref TP/3 (519)

Ministry of Agriculture, Fisheries and Food
Salmon and Freshwater Fisheries Laboratory, London

Biologist

■ In section carrying out a study of factors affecting salmon population ■ Analysis of data obtained from field experiments ■ Based in London ■ Appreciable amount of field work in the provinces.

☐ Degree/HNC or equivalent in biological subject ☐ Good working knowledge of Statistics ☐ Age under 27 ☐ Appointment as Scientific Officer (£1493–£2352) ☐ Ref SB/5/AD ☐ Closing date 21 September 1973

☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service)

British Museum
Research Laboratory, London

Chemist

■ To examine and develop conservation methods for a wide range of organic objects, particularly library and archival material.

☐ 1st or 2nd honours degree or equivalent in Chemistry, with at least 2 years' research experience ☐ Interest in microbiology an advantage ☐ Age normally under 30 ☐ Appointment as Higher Scientific Officer (£2251–£2842) ☐ Ref SB/1/DJA ☐ Closing date 21 September 1973

☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service)

Science group
CIVIL SERVICE

(524)

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)

A STATISTICIAN is required to assist in the analysis of agricultural and biological experiments Knowledge of computer programming would be an advantage

Applicants should have a degree in Statistics, HNC or similar qualification Appointment will be in the grade of Scientific Officer (£1,318 to £2,177) or Higher Scientific Officer (£2,076 to £2,667), with a starting point dependent on qualifications and experience A minimum of five years post-qualifying experience is required for appointment in the higher grade There is a superannuation scheme with a 5½% allowance to offset contributions

Apply on forms obtainable from the Secretary, N I R D, Shinfield, Reading, RG2 9AT Quote reference 73/37 (481)

UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

RESEARCH ASSISTANT required by Reader in Surgery at this Medical School Graduate B Sc in Biological Sciences with a preference to Pharmacology to work on Bio Assay of Gastrin 2-year appointment in the first instance Salary £1,527 in the first year rising to £1,590 in the second year Applications in writing giving details of qualifications to the Secretary, University College Hospital Medical School, University Street, London WC1E 6JJ, quoting reference JW/SU (491)

INSTITUTE OF CLINICAL RESEARCH
MIDDLESEX HOSPITAL MEDICAL SCHOOL

RESEARCH ASSISTANT/ TECHNICIAN

A Research Assistant/Technician is required for a new project involving the measurement of radio-immunoassay of hormones relevant to arterial hypertension Previous experience desirable Please apply to The Secretary (N), Institute of Clinical Research, 32-48 Hanson Street, London, W 1 (531)

UNIVERSITY OF SHEFFIELD
LECTURER
IN THE DEPARTMENT OF BUILDING SCIENCE IN THE FACULTY OF ARCHITECTURAL STUDIES

Applications are invited for the post of Lecturer in the above Department to join a scientific team concerned with environmental design in architecture and planning, and to specialise in architectural aerodynamics and fluid mechanics Candidates must have a good honours degree in an appropriate field of engineering or science, and preferably research experience in the field of applied fluid mechanics/aerodynamics Salary in the range £1,929-£4,548 with FSSU provision Further particulars from the Registrar and Secretary, the University, Sheffield S1[illegible] 2TN, to whom applications (5 copies) should be sent by September 20, 1973 (483)

THE MACAULAY INSTITUTE FOR SOIL RESEARCH
DEPARTMENT OF PEDOLOGY

Applications are invited for two SCIENTIFIC OFFICER/HIGHER SCIENTIFIC OFFICER POSTS to undertake work concerned with the survey and classification of peat and peat lands Candidates should possess a First or Upper Second Class Honours Degree, or a Higher Degree Salary £1,590 to £2,177 per annum (Scientific Officer) or £2,076 to £2,667 per annum (Higher Scientific Officer) according to qualifications and experience Superannuation under F S S U for which a non-pensionable allowance of 4¼% is added to salary to offset contributions

One post (Ref 73/19) is for an Officer to undertake systematic Peat Survey for which a degree with an ecological bias would be appropriate

The other post (Ref 73/20) is more specifically concerned with mapping and air-photo interpretation and requires a degree in Geography or a related subject

Forms of application may be obtained from the Secretary, The Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen AB9 2QJ, to whom they should be returned before September 14, 1973 (513)

IMPERIAL COLLEGE
RESOURCE MANAGEMENT

Applications are invited for a

Postdoctoral Research Assistantship

in The Environmental Resource Management Unit of The Department of Zoology The unit, which is based at the College Field Station, was set up by a grant from The Ford Foundation to carry out research on the application of systems analysis and computer simulation techniques to problems in the management of living resources, especially with respect to the developing countries The chosen candidate will be selected on the basis of his research experience and will be free to carry out any research which falls within the general objective of the unit The post is available from October 1, 1973 (or other date to be arranged) and is tenable for one year, carrying a salary of £1,929 to £2,058 per annum with F S S U membership

Applications accompanied by curriculum vitae, details of research experience and the names of two referees, to Professor T R E Southwood, Imperial College Field Station, Silwood Park, Ascot, Berks, by September 31, 1973 (500)

FACULTY OF MEDICINE
MEMORIAL UNIVERSITY OF NEWFOUNDLAND

Applications are invited for the position of ASSOCIATE DEAN of BASIC MEDICAL SCIENCES at Memorial University in St John's, Newfoundland

The person appointed would be expected to assist in developing the general policies and areas of emphasis of the Medical School and, in particular the Basic Sciences, ensuring that these policies are reflected in faculty recruitment and other activities Preference will be given to candidates who have had considerable research and administrative experience

The duration of the appointment will normally be for a period of three years The post will carry an appropriate academic rank and tenure in accordance with university regulations Salary will be according to qualifications and experience

Applications, accompanied by a detailed curriculum vitae and the names of three referees will be received until November 15, 1973, by either Dean Ian E Rusted or Dr B H Sells, Selection Committee, Faculty of Medicine, Memorial University of Newfoundland, St John's, Newfoundland, Canada (544)

UNIVERSITY OF WALES
THE WELSH NATIONAL SCHOOL OF MEDICINE
Department of Haematology
SCIENTIFIC OFFICER

A Biochemist with experience in protein synthesis is required to join a unit studying the characterization and synthesis of iron containing proteins by mammalian cells Salary will be in the range £1,566 to £2,370 per annum or £2,613 to £3,375 according to age, qualifications and experience

Further details available from the Registrar, The Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN (539)

MEMORIAL UNIVERSITY of Newfoundland — Applications are invited for a faculty position now open in Electron Microscopy Responsibilities include daily supervision of the EM Unit, independent and collaborative research, limited teaching Rank and salary negotiable Interested persons send curriculum vitae and 3 references to Dr C Pfeiffer, Faculty of Medicine, Memorial University of Newfoundland, St John's, Newfoundland, Canada (537)

POSITIONS OPEN

THE UNIVERSITY OF CHICAGO

DEPARTMENT OF ANTHROPOLOGY

seeks for possible appointment at any level, candidates for creative research and imaginative teaching in physical anthropology (human evolution, human biology, biological bases of behaviour, comparative primate studies, other) Since its charter, the principle of the University has been to appoint without regard to race, religion, sex, or national origin Candidates desiring consideration should send vita and documents demonstrating distinction or potential for distinction to Chairman, 1126 East 59th Street, Chicago, IL 60637 (543)

CLINICAL NEUROPHYSIOLOGY RESEARCH ASSISTANT

There is a vacancy for a woman biological sciences graduate in a department concerned with clinical electroencephalography and electromyography and research in related fields There are some routine duties, but the holder will assist in current research and there could be opportunity to work for a higher degree

Salary scale £1,278 to £1,980, according to qualifications, plus £126 London Weighting Allowance

Applications to Dr W A Cobb, Department of Applied Electrophysiology, National Hospital, Queen Square, London, W C 1 (518)

Overseas Development Administration
Tropical Products Institute, London

Biologist/Biochemist

■ Work on the post-harvest physiology and biochemistry of fruits and vegetables of tropical origin in relation to their storage life and quality ■ Day-to-day supervision of laboratory ■ Possibility of work overseas in field conditions.

□ 1st or 2nd honours degree in appropriate subject □ Experimental ability in work with plant materials using modern research techniques □ Age under 32 □ Appointment as Higher Scientific Officer (£2251–£2842) or Senior Scientific Officer (£2790–£3815) □ Ref. SA/3/JD □ Closing date 21 September 1973.

□ Application forms from Administrative Secretary, Tropical Products Institute, 127 Clerkenwell Road, London EC1R 5DB.

Overseas Development Administration
Tropical Products Institute
Industrial Development Department, Culham, Berks

Wood Scientist

■ To join multidisciplinary team studying problems of industrial utilisation of cellulose materials of tropical origin ■ Emphasis on use of forest products and agricultural residues for manufacture of low cost building components ■ Essentially chemical approach to work ■ Possibility of overseas assignments.

□ Degree/HNC or equivalent in Wood Science, Chemistry or Timber Technology □ Age under 27 □ Appointment as Scientific Officer (£1318–£2177) □ Ref SA/2/JD □ Closing date 21 September 1973

□ Application forms from the Administration Officer, Tropical Products Institute, Culham, Abingdon, Berks

Ministry of Agriculture, Fisheries and Food
Royal Botanic Gardens, Kew

Guide Lecturer

■ To conduct tours of school children, students and adults around the Gardens and Museums ■ Lecture to outside bodies ■ Assist in the correspondence and general curatorial matters of the museum department.

□ Degree/HND or equivalent in Botany, Biology or Geography □ Age under 30 □ Appointment as Higher Scientific Officer (£2166–£2757) □ Ref SB/2/AH □ Closing date 21 September 1973

□ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext. 500 or London 01-839 1992 (24 hour answering service).

Science group
CIVIL SERVICE

(525)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS AL5 2JQ

SCIENTIFIC OFFICER or HIGHER SCIENTIFIC OFFICER required for Field Experiments Section Duties include the following preparation and editing of publications describing the general agricultural work of the Station, conducted tours of the Station and demonstrations of field experiments for scientists, farmers and members of the general public , some lecturing on the history and work of the Station and participation in the work of the Section

Appointment in grade of SO (£1,318-£2,177) or HSO (£2,076-£2,667) according to qualifications and experience A relevant degree or equivalent qualification (e g HNC) is required, plus practical knowledge of agriculture At least five years' post qualifying experience is normally required for appointment as HSO Superannuation with allowance of 5½% to offset contributions

Applications, naming two referees and quoting reference 1962, to the Secretary by September 28, 1973 (485)

RESEARCH TECHNICIAN REQUIRED TO work on Interferon synthesis in animal cell culture The appointment, for one year in the first instance, is on an M R C grant Experience in cell culture, biochemistry or virology is desirable Applications to Dr M J Morgan, Department of Biochemistry, University of Leicester, Leicester LE1 7RH (490)

UNIVERSITY OF MALAYA

FACULTY OF SCIENCE

DEPARTMENT OF PHYSICS

Applications are invited for one post of LECTURER/ASSISTANT LECTURER in the Department of Physics Subject to academic suitability and experience, preference will be given to candidate competent in Bahasa Malaysia (Malay) Candidates should have at least a good Honours degree with suitable teaching and research experience For the Lectureship, a doctorate is normally required

Emoluments (Approximate sterling equivalents per annum) are

(i) **Salary Scales**

Lecturers £1,524 by £73 to £1,962/£2,035 by £81 to £2,441

Assistant Lecturers £1,330 by £65 to £1,460

(ii) In addition a Variable Allowance is at present payable at the following rates 35% of basic salary subject to certain maxima depending on marital status minimum £243 per annum, maximum £649 per annum

(iii) Supplementary Housing Allowance of £503 per annum

Medical benefits are provided under the Medical Services Scheme of the University

Further particulars, details of superannuation, and application forms are obtainable from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

The closing date for the receipt of applications is **27 September 1973** (508)

TECHNICIAN

required by the Medical Research Council Unit and Department of Clinical Pharmacology, University of Oxford, Radcliffe Infirmary, Oxford Applicants should have the HNC or AIMLT or equivalent qualification and experience in biochemistry and/or pharmacology The work in the Unit will be biochemical and pharmacological with clinical application Salary will be within the scale £1,335 to £2,154 Applications should be sent to Professor D G Grahame-Smith (512)

UNIVERSITY COLLEGE CARDIFF

(Re-advertisement)

Applications are invited for the following vacancy in the Department of Botany

ASSISTANT EXPERIMENTAL OFFICER OR EXPERIMENTAL OFFICER

to establish and operate a radiocarbon dating laboratory for palaeobotanical and archaeological research Applicants should have experience in vacuum techniques and low-level counting

Qualifications should be in Chemistry or Physics

Salary range £1,764 to £2,874/£3,033 to £3,351

Duties to commence as soon as possible after October 1, 1973

Applications together with the names of two referees, should be forwarded to the Registrar, University College, P O Box 78, Cardiff CF1 1XL, no later than September 19, 1973 Please quote 0891 (489)

Overseas Appointment

This appointment is wholly financed by the British Government under Britain's programme of aid to the developing countries

TECHNICAL ASSISTANT

To be a member of a Plant Research Team studying viruses of maize and tropical legumes The post will be concerned with isolation of viruses, their biochemical and biophysical characteristics, field ecology and control by means of varietal resistance or tolerance Applicants who should normally be citizens of, and permanently resident in, the UK should be over 21 years and preferably single with a degree. HNC or equivalent, in virology, botany or relevant subject. Appointment for 2½–3 years

Salary, subject to UK income tax, in range of £2,035-£2,870 per annum plus a variable tax free overseas allowance in range of £465-£1,130 per annum

Other benefits include free family passages, paid leave, children's education allowances and free accommodation and medical attention

For full details, application form and booklet about Kenya, please apply, giving age and brief details of qualifications and experience, to

Appointments Officer,
Foreign and Commonwealth Office,

**Overseas Development
Administration**

Room E301/N, Eland House, Stag Place,
London SW1E 5DH (468)

Universiteit van Amsterdam

At the Subfaculty of Pharmacy the following post is vacant

full professor in pharmaceutical chemistry

The emphasis will be on medicinal chemistry and less on pharmaceutical analysis, since a separate readership in this field exists

Teaching comprises theoretical and practical aspects of medicinal chemistry, for undergraduates and graduates in Pharmacy Research can be organized in accordance with the related research groups in the subfaculties of pharmacy and chemistry

Candidates for this post (pharmacists and chemists) and those who want to draw the attention to possible candidates should address themselves to the Dean of the Subfaculty of Pharmacy, Prof Dr P A van Zwieten, Laboratory of Biopharmacy, Roetersstraat 1, Amsterdam, Holland

- Final date of application one month after the appearance of this journal

507

UNIVERSITY OF OTAGO

FACULTY OF MEDICINE

CHRISTCHURCH CLINICAL SCHOOL

CHRISTCHURCH—NEW ZEALAND

LECTURER, SENIOR LECTURER OR ASSOCIATE LECTURER IN CLINICAL PHARMACOLOGY

Applications are invited for the above-mentioned appointment at the Christchurch Clinical School Initially Clinical Pharmacology will be one of the divisions of the University Department of Medicine, but it is expected that expansion of activity will take place Clinical Pharmacology will become involved in the educational programme of the School and of the North Canterbury Hospital Board, commencing with the 5th year class in 1974 It is hoped that the successful applicant will take up his duties as soon as possible

Salary Lecturer a scale from $NZ8,042 to $NZ11,587 per annum with a bar at $NZ9,941 per annum

Senior Lecturer a scale from $NZ11,927 to $NZ13,768 per annum

A particularly well qualified candidate could be appointed with the status of Associate Professor with salary at a point within the range of $NZ14,482 to $NZ15,675 per annum

An allowance for clinical duties may be available in the light of status and duties performed Salary scales are subject to both triennial review and regular cost-of-living adjustments

Further particulars are available from the Secretary-General, Association of Commonwealth Universities (Appts), 36 Cordon Square, London WC1H 0PF, or from the Registrar of the University

Applications close in New Zealand and London on **30 September 1973** (509)

UNIVERSITY OF ADELAIDE

Applications are invited for the following appointments

SENIOR DEMONSTRATOR IN PHYSICS from 1974 Duties will include undergraduate laboratory teaching and responsibility for operation of one of the undergraduate laboratories, including supervision of laboratory staff, training of part-time demonstrators and assistance with design and construction of new experiments Participation in research programmes will also be encouraged (21 9 73)

SENIOR LECTURER IN ANATOMY AND HISTOLOGY Registrable medical qualifications desirable but not essential The Department teaches students of medicine, dentistry, science, physiotherapy and occupational therapy Research fields are neuro-endocrinology (using electrophysiological and electron microscopic techniques), human and comparative neurology, cell biology (including cytochemistry), experimental embryology and clinical anatomy (28 9 73)

Salary scales Senior Lecturer $A12,268 by $408(5) to $14,308, Senior Demonstrator $A7,270 by $286(3) by $285(2) to $8,698, with superannuation on the F S S U basis In the Faculty of Medicine special additional allowances are payable for medical qualifications registrable in South Australia (currently under review)

Further particulars about these posts and the conditions of appointment and other information sought will be supplied on request to the Registrar of the University, or to the Secretary-General, Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF

Applications should be sent in duplicate and giving the information listed in Statement that will be supplied, to the Registrar, the University of Adelaide, North Terrace, Adelaide, South Australia 5001 (498)

The University of Leeds

THE HOULDSWORTH SCHOOL OF APPLIED SCIENCE DEPARTMENT OF CERAMICS

Applications are invited for the CHAIR and Headship of the Department of Ceramics made vacant by the resignation of Professor J P Roberts on his appointment to the Dyson Chair in the University of Sheffield

The salary will be not less than £5,625 a year The University reserves the right to consider for appointment persons other than those who submit formal applications

Applications (two copies) stating age, qualifications and experience, and naming three referees, should reach the Registrar, The University, Leeds LS2 9JT, quoting the reference number 34/12/D not later than November 30, 1973 Applicants from overseas may apply in the first instance by cable naming three referees, who should preferably be in the United Kingdom (502)

Glaxo

Microbiologist

Fermentation Development Department *Ulverston*

We wish to appoint a qualified Microbiologist to a position which offers a wide scope in microbiological problems associated with the production of antibiotics and enzymes This work is essentially inter-disciplinary and the person appointed will be part of a team, which has close contacts with specialists in other fields such as biochemistry, biochemical engineering and genetics

Academic and/or industrial experience in the field of microbial strain development using mutation, biochemical and genetical techniques would be an asset

Salary will reflect the responsibility of the appointment Features of employment are attractive and include participation in the Glaxo Group Bonus and Pension Schemes Assistance with relocation expenses will be given where appropriate

Ulverston is a market town situated in North Lancashire on the fringe of the National Park Area of the Lake District

Please write stating age, qualifications and experience to The Personnel Officer (JE), Glaxo Laboratories Limited, North Lonsdale Road, Ulverston, Lancashire (516)

GRADUATE RESEARCH ASSISTANT and JUNIOR TECHNICIAN required in THE TISSUE CULTURE AND CYTOGENETICS UNIT Relevant experience desirable but not essential as adequate training will be given Applications with the names of two referees should be made to Dr D C Williams, Research Department, Marie Curie Foundation, The Chart, Oxted, Surrey, by September 7 (427)

UNIVERSITY OF ABERDEEN

RESEARCH ASSISTANT required from October 1, 1973, for the Unit for Research on Addictive Drugs Minimum qualifications Second Class Honours Degree in Pharmacology, Physiology or Pharmacy Salary on scale £1,305×87—£1,479×90—£1,659 with placing according to qualifications Appointment for one year in first instance, renewable for two further years Enrolment for a Higher Degree will be encouraged

The research project deals with the assessment of the potencies of new narcotic analgesic drugs, their structure-activity relationships and the development of new assay methods

Further particulars from The Secretary, The University, Aberdeen, with whom applications (2 copies) with curriculum vitae and names of two referees should be lodged by Sptember 14, 1973 (394)

FANCY A CHANGE

We have vacancies galore at every grade in the scientific field, including marketing

For further details, write or telephone
WALBROOK APPOINTMENTS,
116 HIGH HOLBORN, LONDON, W C 2
Tel 01-405 8787
(3)

AUSTRALIA

The New South Wales State Cancer Council

THE MEDICAL DIRECTOR

The Council is seeking a Medical Director of The New South Wales State Cancer Council He shall also be in charge of and responsible for the redevelopment of the Special Unit for research into human cancer

The Council has in mind the need for change in character of the Special Unit and for its possible re-development as an institute The nature of these changes will depend on the interests, qualifications and experience of the Medical Director and so the Council does not wish to lay down terms and conditions of appointment which are so explicit that they will restrict the Medical Director after his appointment

Therefore the Council, while outlining the qualifications, as stated hereunder, that it seeks in its Medical Director, is prepared to discuss appropriate variations of these with candidates

Council will welcome enquiries from interested persons who

(a) are medical graduates qualified for registration in New South Wales,

(b) are of clinical professorial status,

(c) have already had substantial experience in cancer research or have demonstrated their potential to direct and conduct such research,

(d) will work full-time with the Council and will be responsible for the general administration of the Council and the Special Unit or Institute,

(e) wish to teach medical and science graduates and undergraduates and to supervise postgraduates

Further enquiries may be made of The Chairman of the New South Wales State Cancer Council, The Vice Chancellor, Sydney University, Sydney 2006 The closing date will be January 31, 1974 (267)

FELLOWSHIPS AND STUDENTSHIPS

UNIVERSITY OF SUSSEX

SCHOOL OF BIOLOGICAL SCIENCES

RESEARCH FELLOWSHIP IN INVERTEBRATE NEUROPHYSIOLOGY

Applications are invited from post-doctoral neurophysiologists to take part in an MRC supported project concerned with the growth and development of the molluscan nervous system

Preference will be given to Ph D s with experience in intracellular recording techniques which may have been obtained on vertebrate or invertebrate animals

The post is available from October 1, 1973, and will last for three years The salary will be in the range £1,764-£2,079 per annum

Further particulars and application forms can be obtained from the Secretary of Science, Science Office (E), University of Sussex, Falmer, Brighton BN1 9RH (379)

UNIVERSITY OF LIVERPOOL

DEPARTMENT OF APPLIED MATHEMATICS AND THEORETICAL PHYSICS

Applications are invited for the post of THEORETICAL PHYSICS RESEARCH FELLOW The salary for the Fellowship will be within the range £1,929-£2,223 per annum, plus FSSU benefits

Applications, stating age, qualifications and experience, together with the names of two referees, should be received not later than September 17, 1973, by the Registrar The University, P O Box 147, Liverpool L69 3BX, from whom further particulars may be obtained Quote Ref RV/N/80436 (457)

UNIVERSITY OF LONDON

INSTITUTE OF PSYCHIATRY DEPARTMENT OF NEUROLOGY

POSTDOCTORAL RESEARCH FELLOWSHIP

Applications are invited from recently qualified doctorates in biochemistry or pharmacology for a study of the biochemical/pharmacological basis of some drug-induced basal ganglia diseases Suitable candidates should preferably have a knowledge of biogenic amine metabolism and be familiar with current physico-chemical methods of analysis

Salary within the range £1,826 to £2,241 including London Allowance renewable annually up to three years

Applications in writing together with curriculum vitae should be sent to the Secretary, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF from whom further details may be obtained, quoting reference PJ/N (532)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF BIOCHEMISTRY

A vacancy exists for a RESEARCH FELLOW with effect from October 1, 1973, for one year in the first instance, normally renewable for a further two years The successful candidate will be required to work in one of the research areas currently of interest to the Department These include biochemistry of contractile systems, enzymology, membrane biochemistry, metabolic regulation, metabolism of foreign organic compounds, microbiology, nucleic acids, protein structures and interactions, lipids, photobiology

Salary £1,764 to £2,079 plus FSSU

Applications naming three referees by September 15, 1973, to the Assistant Registrar (B), University of Birmingham, P O Box 363, Birmingham B15 2TT, from whom further particulars may be obtained (459)

THAMES POLYTECHNIC

SCHOOL OF BIOLOGICAL SCIENCES

Applications are invited for

POST-DOCTORAL RESEARCH FELLOW IN BIOCHEMISTRY

Applications are invited from appropriately qualified persons for the post of Post-Doctoral Research Fellow in the School of Biological Sciences The successful applicant will be required to work on applications of affinity chromatography and related techniques to lipophilic proteins Previous experience with membrane proteins, although not essential, would be an added recommendation

The post, which is financed by the S R C, is of two years' duration and is at a salary of £1,881 by £72 plus London weighting It is hoped to make the appointment with effect from October next

Further particulars and form of application may be obtained from the Secretary, Thames Polytechnic, Wellington Street, London SE18 6PF, to whom completed applications should be returned by September 21, 1973 (535)

UNIVERSITY OF STRATHCLYDE

Department of Biochemistry

M.R.C. RESEARCH SCHOLARSHIP

Applications are invited from suitably qualified graduates in Biochemistry, or cognate subject, with a sound Biochemical background, for the above scholarship This will be concerned with a study of ornithine decarboxylase and related enzymes in reproductive tissues, and will be registrable for a Higher Degree The scholar will be closely associated with the active M R C Group for Research in Biochemistry of Reproduction established in the Department

Applications to Professor P J Heald, Department of Biochemistry, University of Strathclyde, Royal College Building, 204 George Street, Glasgow G1 1XW

(517)

MEDICAL RESEARCH COUNCIL

Clinical and Population Cytogenetics Unit

SCIENTIST

A vacancy for a research scientist will shortly become available in the Cytogenetics Section of the above Unit Applications are invited from graduates with a Ph D , or equivalent, in genetics or cytogenetics and an interest in the effects of environmental mutagens on human and other mammalian chromosomes Salary, dependent upon age, qualifications and experience, will be within the scale £1,688 to £3,192 with FSSU benefits.

Applications in writing, giving full personal particulars and names of two referees, to the Administrative Office, MRC Clinical and Population Cytogenetics Unit, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, by September 14, 1973 (374)

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LIVERPOOL POLYTECHNIC

School of Pharmacy

S R C STUDENTSHIP IN MEDICINAL CHEMISTRY

Applications are invited from candidates with a good honours degree or equivalent in Pharmacy or Chemistry, to work for a higher degree on the project "4-phenypiperidine derivatives as potential non-addicting analgesics"

The project is a CASE award and the co-operating body is Allen and Hanburys Ltd The stipend (£675 per annum maximum plus fees)

Supervisor Dr A F Casy

Details available from Staff Office, Dept. N, Liverpool Polytechnic, Richmond House, 1 Rumford Place, Liverpool L3 9RH. (526)

UNIVERSITY OF CAMBRIDGE

C A P S RESEARCH STUDENTSHIP

Applications are invited for a C A P S research studentship in organic chemistry in association with Beecham's Laboratories, Brockham Park The project involves the synthesis, chemical and biological study of analogues of the antibiotic phosphonomycin, and is expected to lead to a Ph D degree

Applications to Dr S G Warren, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW (499)

UNIVERSITY OF SUSSEX

SCHOOL OF MOLECULAR SCIENCES

POSTDOCTORAL FELLOWSHIP IN CLINICAL CHEMISTRY

Applications are invited for the above post to work in collaboration with a small biomedical group on the application of kinetic methods to the development of automated analytical procedures in clinical biochemistry

The appointment is for one year in the first instance, commencing October 1, 1973, or as soon as possible thereafter Salary dependent upon age and experience in the range £1,929 to £2,223 per annum plus F S S U

Applications with the names and addresses of two referees should be sent to the Sub-Dean, School of Molecular Sciences, University of Sussex, Brighton BN1 9QJ, from whom further information may be obtained (505)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF CLINICAL CHEMISTRY

Applications are invited from BIOCHEMISTS, preferably post-doctoral, for the post of RESEARCH FELLOW/ASSOCIATE to investigate the control of protein synthesis in human and animal tissue by hormones and other agents The project is supported by a grant from the MRC

Salary in the range £1,569 to £2,718 depending on qualifications, age and experience, plus FSSU

Further particulars may be obtained from Dr D R London, Queen Elizabeth Hospital, Birmingham B15 2TH to whom applications (3 copies), naming three referees, should be sent by October 1, 1973 (473)

MONASH UNIVERSITY

DEPARTMENT OF PHYSIOLOGY

(including Pharmacology)

LECTURER, SENIOR TEACHING FELLOW or TEACHING FELLOW

The Department of Physiology conducts courses in Physiology and Pharmacology for B Sc (Hons) and M B , B S degrees and accepts graduate students for M Sc and Ph D degrees Duties will relate especially to Science undergraduate teaching Research interests include brain ultra structure, neurophysiology, biophysics and pharmacology of central and peripheral synapses, muscle biophysics, circulatory physiology and pharmacology, renal and endocrine physiology Applicants for Senior Teaching Fellowship or Lecturer should preferably have a Ph D or medical qualification

Salary scale Lecturer, $A8,698 to $A11,982 per annum with superannuation based on an endowment assurance scheme, the employee and employer contributing 5 per cent and 10 per cent respectively

Senior Teaching Fellow $A7,270 to $A8,698 per annum Teaching Fellow $A5,740 to $A7,015 per annum

Benefits Travelling expenses for appointee and family, removal allowance, repatriation after three years' appointment if desired, temporary housing for

C.A.S.E. Studentships

Applications are invited from graduates with a good Honours Degree in Materials Science, Metallurgy, Physics, Chemistry, Engineering, etc, for a Science Research Council Studentship, normally tenable for three years, from October 1, 1973, to study for the D Phil degree The work involves the study of damage produced in metals by heavy ion irradiation using transmission electron microscopy at high and low temperatures The studentship is under the scheme of Cooperative Awards in Science and Engineering, and the student will spend a considerable fraction of his time using special equipment at the Atomic Energy Research Establishment, Harwell

Candidates should apply, as soon as possible, giving a brief curriculum vitae and the names of two referees, to the Administrator, Department of Metallurgy, Parks Road, Oxford OX1 3PH

(466)

Tumour Virology

The Searle Group, a leading research based company in the pharmaceutical industry, require a BIOCHEMIST or CELL BIOLOGIST with an interest in virology to lead a group developing new therapies for animal leukaemias

The work will lead to a practical application of recent advances in the knowledge of RNA tumour viruses and it is intended that this will be an expanding activity within the Company

The group will be fully integrated with the existing research departments which are working on many basic aspects of molecular biology

The person appointed should preferably have a PhD in biochemistry, cell biology or virology

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